METHODS AND COMPOSITIONS RELATING TO GRADIENT EXPOSED CELLS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims priority to U.S. Application Serial No. 60/431,424 filed December 6, 2003, U.S. Application Serial No. 60/438,848 filed January 9, 2003, and U.S. Application Serial No. 60/445,049 filed February 5, 2003.

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This work was supported by NIH grants R21 A145898-01. The government may have certain rights to the invention.

FIELD OF THE INVENTION

The invention is directed to methods and compositions relating to modulation of gene expression in cells in chemotactic and fugetactic gradients.

BACKGROUND OF THE INVENTION

Cell movement in response to specific stimuli occurs in prokaryotes and eukaryotes (Doetsch RN and Seymour WF.,1970; Bailey GB et al.,1985). Cell movement by these organisms has been classified into three types; chemotaxis, which is cell movement along a gradient towards an increasing concentration of an agent (e.g., a chemical); negative chemotaxis, which is cell movement towards a decreasing concentration of an agent, and chemokinesis, which is the random movement of cells.

The receptors and signal transduction pathways affected by the actions of specific chemotactically active compounds have been extensively defined in prokaryotic cells. Study of E. coli chemotaxis has revealed that a chemical which attracts the bacteria at some concentrations and conditions may also act as a repellant at others (i.e., a "negative chemotactic chemical" or "chemorepellent") (Tsang N et al., 1973; Repaske D and Adler J. 1981; Tisa LS and Adler J.,1995; Taylor BL and Johnson MS., 1998).

Chemotaxis and chemokinesis have been observed to occur in mammalian cells (McCutcheon MW, Wartman W and HM Dixon, 1934; Lotz M and H Harris; 1956; Boyden SV 1962) in response to the class of proteins, called chemokines (Ward SG and Westwick J; 1998; Kim CH et al., 1998; Baggiolini M, 1998; Farber JM; 1997). Chemokines induce cell motion by signaling through G-protein coupled receptors (Wells TN et al., 1998).

G-protein coupled receptors include a wide range of biologically active receptors, such as hormone, viral, growth factor and neuroreceptors. The G-protein family of coupled receptors includes dopamine receptors, which bind to neuroleptic drugs used for treating psychotic and neurological disorders. Other examples of members of this family include calcitonin, adrenergic, endothelin, cAMP, adenosine, muscarinic, acetylcholine, serotonin, histamine, thrombin, kinin, follicle stimulating hormone, opsins, endothelial differentiation gene-1 receptor, rhodopsins, odorant, cytomegalovirus receptors, etc.

G-protein coupled receptors have been characterized as having seven putative transmembrane domains, designated as transmembrane domains 1-7

("TM1," "TM2," "TM3," "TM4," "TM5," "TM6," and "TM7"). The domains are believed to represent transmembrane α-helices connected by extracellular or cytoplasmic loops. In each of the first two extracellular loops, most G-protein coupled receptors have single conserved cysteine residues forming disulfide bonds that are believed to stabilize functional protein structure. Phosphorylation (as well as lipidation, e.g., palmitylation or farnesylation) can influence signal transduction and potential phosphorylation sites lie within the third cytoplasmic loop and/or the carboxy-terminus. For several G-protein coupled receptors, such as the β-adrenoreceptor, phosphorylation by protein kinase A and/or specific receptor kinases mediates receptor desensitization.

Phosphorylation of cytoplasmic residues of G-protein coupled receptors has been identified as an important mechanism for the regulation of G-protein coupling. G-protein coupled receptors can be intracellularly coupled by heterotrimeric G-proteins to various intracellular enzymes, ion channels and transporters (see, Johnson et al., Endoc Rev, 1989, 10:317-331). Different G-protein α-subunits preferentially stimulate particular effectors to modulate various biological functions in a cell. This signaling pathway can be blocked, for example, by pertussis toxin (PTX) (Luster AD, 1998; Baggiolini, 1998).

As discussed above, chemokine-induced cell chemotaxis is mediated via a $G_{\alpha i}$-linked signal transduction pathway. The chemokine, SDF-1α, provides one example of this signaling model. SDF-1α, causes immigration of subpopulations of leukocytes into sites of inflammation (Aiuti A et al. 1997; Bleul CC et al. 1996; Bleul CC et al., 1996; Oberlin E et al., 1996). Furthermore, mice engineered to be deficient in SDF-1α or its receptor, CXCR-4, have abnormal development of hematopoietic tissues and B-cells due to the failure of fetal liver stem cells to migrate to bone marrow (Friedland JS, 1995; Tan J and Thestrup-Pedersen K, 1995; Corrigan CJ and Kay AB, 1996; Qing M, et al,1998; Ward SG et al. 1998). This movement is concentration-dependent, and is mediated via the CXCR4 receptor, Gαi protein and PI-3 kinase (Nature Medicine 2000; 6,543). The switch from a chemotactic to a fugetactic response in T cells is associated with intracytoplasmic levels of cyclic nucleotides and a differential sensitivity to tyrosine kinase inhibitors.

Methods for identification of the genes involved in modulation of cell movement through a gradient (e.g., genes involved in relevant $G_{\alpha i}$-linked signal

transduction pathways) have not been performed. Such methods would be useful for the identification of new therapeutic targets in diseases characterized by aberrant cellular movement.

SUMMARY OF THE INVENTION

The invention is premised, in part, on the discovery that exposure of cells to a gradient results in changes in the gene expression profile of such cells. In addition, it has been unexpectedly found that movement of a cell through a gradient also induces changes in gene expression. In some cases, the gradients exist across the diameter of a cell such that the leading most edge of a cell is exposed to a different concentration of agent than is the lagging edge of the cell.

Thus, in one aspect, the invention provides a method for identifying a nucleic acid expressed in a concentration dependent manner, comprising determining a first nucleic acid expression profile of a first cell at a first position in an agent concentration gradient, determining a second nucleic acid expression profile of a second cell at a second position in the agent concentration gradient, and determining a difference between the first and second nucleic acid expression profiles. The first position in the agent concentration gradient corresponds to a first concentration of agent, and the second position in the agent concentration gradient corresponds to a second concentration of agent. Preferably, the second cell was genetically identical to the first cell prior to migration through the agent concentration gradient.

In some embodiments, at least the second cell has migrated through the agent concentration gradient. Therefore, the invention provides a method for identifying a nucleic acid expressed in a concentration dependent manner, comprising determining a first nucleic acid expression profile of a first cell at a first position in an agent concentration gradient, determining a second nucleic acid expression profile of a second cell that has migrated through the agent concentration gradient, and determining a difference between the first and second nucleic acid expression profiles.

In other embodiments, the neither cell has migrated through the agent concentration gradient, but at least the second cell is present in a gradient such that the agent concentration at one end of the cell is different from the agent concentration at the opposite end of the cell.

In one embodiment, the nucleic acid expression profile is a mRNA expression profile. In another embodiment, the mRNA expression profile is determined using PCR, RDA, Northern analysis, subtractive hybridization, or microarray analysis.

In one embodiment, the agent concentration gradient is a ligand concentration gradient. In another embodiment, the agent concentration gradient is a chemokine concentration gradient.

In yet another embodiment, the chemokine concentration gradient is selected from the group consisting of SDF-1α, SDF-1β, IP-10, MIG, GROα, GROβ, GROγ, IL-8, PF4, MCP, MIP-1α, MIP-1β, MIP-1γ (mouse), MCP-2, MCP-3, MCP-4, MCP-5 (mouse), RANTES, fractalkine, lymphotactin, CXC, IL-8, GCP-2, ENA-78, NAP-2, IP-10, MIG, I-TAC, SDF-1α, BCA-1, PF4, Bolekine, HCC-1, Leukotactin-1 (HCC-2, MIP-5), Eotaxin, Eotaxin-2 (MPIF2), Eotaxin-3 (TSC), MDC, TARC, SLC (Exodus-2, 6CKine), MIP-3α (LARC, Exodus-1), ELC (MIP-3β), I-309, DC-CK1 (PARC, AMAC-1), TECK, CTAK, MPIF1 (MIP-3), MIP-5 (HCC-2), HCC-4 (NCC-4), C-10 (mouse), C Lymphotactin, and CX_3C Fracktelkine (Neurotactin) and ITAC concentration gradients.

The agent concentration gradient may be a cytokine concentration gradient. The cytokine concentration gradient may be selected from the group consisting of PAF, N-formylated peptides, C5a, LTB_4 and LXA_4, chemokines: CXC, IL-8, GCP-2, GRO, GROα, GROβ, GROγ, ENA-78, NAP-2, IP-10, MIG, I-TAC, SDF-1α, BCA-1, PF4, Bolekine, MIP-1α, MIP-1β, RANTES, HCC-1, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5 (mouse), Leukotactin-1 (HCC-2, MIP-5), Eotaxin, Eotaxin-2 (MPIF2), Eotaxin-3 (TSC), MDC, TARC, SLC (Exodus-2, 6CKine), MIP-3α (LARC, Exodus-1), ELC (MIP-3β), I-309, DC-CK1 (PARC, AMAC-1), TECK, CTAK, MPIF1 (MIP-3), MIP-5 (HCC-2), HCC-4 (NCC-4), MIP-1γ (mouse), C-10 (mouse), C Lymphotactin, and CX_3C Fracktelkine (Neurotactin) concentration gradients. The cytokine can be a member of the Cys-X-Cys family of chemokines (e.g., chemokines that bind to the CXCR-4 receptor). Preferred cytokines of the invention include SDF-1α, SDF-1β, met-SDF-1β, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-10, IL-12, IL-15, IL-18, TNF, IFN-α, IFN-β, IFN-γ, granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating

factor (G-CSF), macrophage colony stimulating factor (M-CSF), TGF-β, FLT-3 ligand, VEGF, DMDA, endothelin, and CD40 ligand.

In one embodiment, the first concentration of agent is a zero concentration of agent, and the second concentration of agent is a non-zero concentration of agent. In another embodiment, the first concentration of agent is greater than the second concentration of agent.

In one embodiment, the first cell has migrated through the agent concentration gradient. The migration through the agent concentration gradient may be fugetactic migration or chemotactic migration.

In one embodiment, the gradient is a step gradient. In another embodiment, the gradient is a continuous gradient. In yet another embodiment, the method further comprises a combination gradient, wherein at least one additional gradient co-exists with the first gradient.

In one embodiment, the first and second cells are adult cells. In preferred embodiments, the first and second cells are human cells. In one embodiment, the first and second cells are primary cells. In another preferred embodiment, first and second cells are hemopoietic cells, such as but not limited to T lymphocytes.

In another aspect, the invention provides a method for identifying a compound that can modulate cell migration in one or more agent concentration gradients comprising contacting a migratory cell in an agent concentration gradient with a test compound, determining the nucleic acid expression profile in the cell and identifying a change in expression of a gene expression product. Cell movement can be chemotaxis or fugetaxis and therefore, the gene expression product can be a chemotaxis or fugetaxis specific gene product.

In another aspect, the invention provides a method for inhibiting cell fugetaxis comprising contacting a cell undergoing or likely to undergo fugetaxis with an agent that inhibits a fugetaxis specific gene expression product in an amount effective to inhibit fugetaxis.

In one embodiment, the fugetaxis specific gene expression product is a nucleic acid or a peptide. In another embodiment, fugetaxis specific gene expression product is a signaling molecule. The signaling molecule may be selected from the group consisting of cell division cycle 42, annexin A3, Rap1 guanine nucleotide exchange factor, adenylate cyclase 1, JAK binding protein, and Rho GDP

dissociation inhibitor alpha, but it is not so limited. In another embodiment, the signaling molecule is cell division cycle 42 (cdc42), ribosomal protein S6 kinase, BAI1-associated protein 2, GTPase regulator associated with FAK, protein kinase C-beta 1, phosphoinositide-specific phospholipase C-beta 1, nitric oxide synthase 1, phosphatidylinositol-4-phosphate 5-kinase, and MAP kinase kinase kinase kinase 4.

In another embodiment, the fugetaxis specific gene expression product is an extracellular matrix related molecule. In a related embodiment, the extracellular matrix related molecule may be selected from the group consisting of chitinase 3-like 1 (cartilage glycoprotein-39), carcinoembryonic antigen-related cell adhesion molecule 6, matrix metalloproteinase 8 (neutrophil collagenase), integrin cytoplasmic domain-associated protein 1, ficolin (collagenfibrinogen domain-containing) 1, and lysosomal-associated membrane protein 1, epithelial V-like antigen 1, vascular endothelial growth factor (VEGF), fibulin 1, carcinoembryonic antigen-related cell adhesion molecule 3, but it is not so limited.

In yet another embodiment, the fugetaxis specific gene expression product is a cytoskeleton related molecule. The cytoskeleton related molecule may be selected from the group consisting of ankyrin 1 (erythrocytic), S100 calcium-binding protein A12 (calgranulin C), plectin 1 (intermediate filament binding protein, 500kD), and ankyrin 2 (neuronal), microtubule-associated protein RPEB3, microtubule-associated protein 1A like protein (MILP), capping protein (actin filament, gelsoline-like), but it is not so limited.

In still another embodiment, the fugetaxis specific gene expression product is a cell cycle molecule. The cell cycle molecule may be selected from the group consisting of v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog, lipocalin 2 (oncogene 24p3), lectin, (galactoside-binding, galectin 3), RAB31 (member RAS oncogene family), disabled (Drosophila) homolog 2 (mitogen-responsive phosphoprotein), RAB9 (member RAS oncogene family, pseudogene 1), and growth differentiation factor 8, but it is not so limited.

In a further embodiment, the fugetaxis specific gene expression product is an immune response related molecule. The immune response related molecule may be selected from the group consisting of major histocompatibility complex (class II, DR alpha), S100 calcium-binding protein A8 (calgranulin A), small inducible cytokine subfamily A (Cys-Cys), eukaryotic translation initiation factor 5A, small inducible

cytokine subfamily B (Cys-X-Cys) (member 6, granulocyte chemotactic protein 2), Fc fragment of IgG binding protein, CD24 antigen (small cell lung carcinoma cluster 4 antigen), cytochrome P450 (subfamily IVF, polypeptide 3, leukotriene B4 omega hydroxylase), MHC class II transactivator, T cell receptor (alpha chain), T cell activation (increased late expression), MKP-1 like protein tyrosine phosphatase, T cell receptor gamma constant 2, T cell receptor gamma locus, but it is not so limited.

In a further embodiment, the fugetaxis specific gene expression product is chemokine (C-X3-C) receptor 1.

In another aspect, the invention provides a method for inhibiting cell chemotaxis comprising contacting a cell undergoing or likely to undergo chemotaxis with an agent that inhibits a chemotaxis specific gene expression product in an amount effective to inhibit chemotaxis.

In one embodiment, the chemotaxis specific gene expression product is a nucleic acid or a peptide. In another embodiment, the cell is an immune cell.

In one embodiment, the contacting occurs in vivo in a subject having or at risk of having an abnormal immune response. In one embodiment, the abnormal immune response is an inflammatory response. In another embodiment, the abnormal immune response is an autoimmune response. The autoimmune response may be selected from the group consisting of rheumatoid arthritis, Crohn's disease, multiple sclerosis, systemic lupus erythematosus (SLE), autoimmune encephalomyelitis, myasthenia gravis (MG), Hashimoto's thyroiditis, Goodpasture's syndrome, pemphigus (e.g., pemphigus vulgaris), Grave's disease, autoimmune hemolytic anemia, autoimmune thrombocytopenic purpura, scleroderma with anti-collagen antibodies, mixed connective tissue disease, polymyositis, pernicious anemia, idiopathic Addison's disease, autoimmune-associated infertility, glomerulonephritis (e.g., crescentic glomerulonephritis, proliferative glomerulonephritis), bullous pemphigoid, Sjögren's syndrome, insulin resistance, and autoimmune diabetes mellitus, but it is not so limited. In still another embodiment, the abnormal immune response is a graft versus host response.

In one embodiment, the chemotaxis specific gene expression product is a signaling molecule. In a related embodiment, the signaling molecule is selected from the group consisting of G protein-coupled receptor kinase 6, vaccinia related kinase 1, PTK2 protein tyrosine kinase 2, STAM-like protein containing SH3 and

ITAM domains 2, signal-induced proliferation-associated gene 1, CD47 antigen (Rh-related antigen, integrin-associated signal transducer), and protein tyrosine phosphatase (non-receptor type 12). In another related embodiment, the signaling molecule is selected from the group consisting of PTK2 (focal adhesion kinase), MAP kinase kinase kinase kinase 2, guanine nucleotide binding protein, PT phosphatase (receptor), cdc42-binding protein kinase beta, Ral GEF (RalGPS1A), MAP kinase 7, autotaxin, inositol 1,4,5-triphosphate receptor, phosphoinositide-3-kinase gamma, PT phosphatase (non-receptor), RAS p21 protein activator (GAP), RAS guanyl releasing protein 2, and Arp23 complex 20kDa subunit.

In one embodiment, the chemotaxis specific gene expression product is a extracellular matrix related molecule. In a related embodiment, the extracellular matrix related molecule is selected from the group consisting of spondin 1 (f-spondin, extracellular matrix protein), collagen type XVIII (alpha 1), CD31 adhesion molecule, tetraspan 3, glycoprotein A33, and angio-associated migratory cell protein.

In one embodiment, the chemotaxis specific gene expression product is a cytoskeleton related molecule. In a related embodiment, the cytoskeleton related molecule is selected from the group consisting of actin related protein 23 complex (subunit 4, 20 kD), tropomyosin 2 (beta), SWISNF related matrix associated actin dependent regulator of chromatin (subfamily a, member 5), spectrin beta (non-erythrocytic 1), myosin (light polypeptide 5, regulatory), keratin 1, plakophilin 4, and capping protein (actin filament, muscle Z-line, alpha 2).

In one embodiment, the chemotaxis specific gene expression product is a cell cycle molecule. In a related embodiment, the cell cycle molecule is selected from the group consisting of FGF receptor activating protein 1, v-maf musculoaponeurotic fibrosarcoma (avian) oncogene homolog, cyclin-dependent kinase (CDC2-like) 10, TGFB inducible early growth response 2, retinoic acid receptor alpha, anaphase promoting complex subunit 10, RAS p21 protein activator (GTPase activating protein, 3-Ins-1,3,4,5,-P4 binding protein), cell division cycle 27, programmed cell death 2, c-myc binding protein, mitogen-activated protein kinase kinase kinase 1, TGF beta receptor III (betaglycan, 300 kDa), and G1 to S phase transition 1.

In one embodiment, the chemotaxis specific gene expression product is an immune response related molecule. In a related embodiment, the immune response related molecule is selected from the group consisting of major histocompatibility complex class II DQ beta 1, bone marrow stromal cell antigen 2, Burkitt lymphoma receptor 1 (GTP binding protein, CXCR5), CD7 antigen (p41), Stat2 type a, T cell immune regulator 1, and interleukin 21 receptor.

In another aspect, the invention provides a method for promoting cell fugetaxis comprising contacting a cell with a non-chemokine agent that promotes fugetaxis in an amount effective to promote fugetaxis. In one embodiment, the contacting occurs in vivo in a subject having a disorder characterized by lack of fugetaxis. In one embodiment, the cell is a hematopoietic cell, such as a T lymphocyte. In another embodiment, the cell is a neural cell.

In another aspect, the invention provides a method for promoting cell chemotaxis comprising contacting a cell with a non-chemokine agent that promotes chemotaxis in an amount effective to promote chemotaxis. In one embodiment, the contacting occurs in vivo in a subject having a disorder characterized by lack of chemotaxis. In another embodiment, the cell is a hematopoietic cell, such as a T lymphocyte. In another embodiment, the cell is a neural cell.

The invention is also premised in part on various other findings. These include the finding that neutrophils migrate bi-directionally in response to IL-8. That is, neutrophils respond to low concentrations of IL-8 (e.g., 10 ng/ml to 500 ng/ml) by undergoing chemotaxis. Neutrophils respond to high concentration of IL-8 (e.g., 1 microgram/ml to 10 microgram/ml) by undergoing fugetaxis. Accordingly, the invention provides methods for modulating neutrophil migration by modulating the concentration of IL-8.

In one embodiment, the invention provides a method for promoting chemotaxis in a neutrophil comprising contacting a cell with IL-8 in an amount effective to promote chemotaxis by the neutrophil. In one embodiment, the contacting occurs in vivo in a subject having a disorder characterized by lack of neutrophil chemotaxis. Disorders characterized by lack of neutrophil chemotaxis include, but are not limited to, bacterial infections and granulomatous diseases (e.g., tuberculosis).

In one embodiment, the invention provides a method for promoting fugetaxis in a neutrophil comprising contacting a cell with IL-8 in an amount effective to promote fugetaxis by the neutrophil. In one embodiment, the contacting occurs in vivo in a subject having a disorder characterized by lack of neutrophil fugetaxis.

Disorders characterized by lack of neutrophil fugetaxis include, but are not limited to, inflammatory or immune mediated diseases, rejection of a transplanted organ or tissue, rheumatoid arthritis, automimmune diseases and asthma.

The invention further provides methods for identifying gene products that are modulated (i.e., either up regulated or down regulated) in response to IL-8 induced fugetaxis or chemotaxis. Thus, in a further aspect, the invention also provides methods for modulating the effects of IL-8 on neutrophils by inhibiting or enhancing the effects of IL-8 induced fugetaxis specific gene products or IL-8 induced chemotaxis specific gene products.

In another embodiment, the invention provides a method for inhibiting neutrophil chemotaxis comprising contacting a neutrophil undergoing or likely to undergo chemotaxis with IL-8 in an amount effective to inhibit or enhance expression of a chemotaxis specific gene expression product. In one embodiment, the contacting occurs in vivo in a subject having or at risk of having an abnormal immune response.

In a further embodiment, the chemotaxis specific gene expression product is an immune response related molecule. The immune response related molecule may be selected from the group consisting of IL-8, GCP-2, Gro-α, Gro β, Gro γ, CINC-1, CINC-2, ENA-78, NAP-2, LIX, SDF-1, IL-1α and IL-1β, C3a, C5a and leukotrienes.

The invention is further premised in part on the finding that IL-8 induced chemotaxis of neutrophils is selectively inhibited by the PIK3 inhibitor wortmannin, causing cells to undergo fugetaxis to all concentrations of IL-8. Accordingly, in one embodiment, the invention provides methods for inhibiting IL-8 induced chemotaxis of neutrophils (conversely enhancing IL-8 induced fugetaxis of neutrophils) by administering to a subject in need thereof an effective amount of wortmannin. The effecive amount of wortmannin is that amount effective to selectively inhibit IL-8 induced chemotaxis of neutrophils and optionally to enhance neutrophil fugetaxis in

the presence of IL-8. The method can also be performed with other species of this genus.

In another embodiment, the invention provides a method for inhibiting neutrophil fugetaxis comprising contacting a neutrophil undergoing or likely to undergo fugetaxis with IL-8 in an amount effective to inhibit or enhance expression of a fugetaxis specific gene expression product. In one embodiment, the contacting occurs in vivo in a subject having or at risk of having an abnormal immune response.

In a further embodiment, the fugetaxis specific gene expression product is an immune response related molecule. The immune response related molecule may be selected from the group consisting of IL-8, GCP-2, Gro-α, Gro β, Gro γ, CINC-1, CINC-2, ENA-78, NAP-2, LIX, SDF-1, IL-1α and IL-1β, C3a, C5a and leukotrienes.

The invention is further premised in part on the finding that IL-8 induced fugetaxis of neutrophils is selectively inhibited by alternative PI3K inhibitor LY294002, causing cells to chemotax to all concentrations of IL-8. Accordingly, in one embodiment, the invention provides methods for inhibiting IL-8 induced fugetaxis of neutrophils (and conversely enhancing IL-8 induced chemotaxis of neutrophils) by administering to a subject in need thereof an effective amount of PI3K inhibitor LY294002. The effective amount of LY294002 is that amount effective to selectively inhibit IL-8 induced fugetaxis of neutrophils and optionally to enhance neutrophil chemotaxis in the presence of IL-8. The method can also be performed with other species of this genus.

These and other objects of the invention will be described in further detail in connection with the detailed description of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

The following Detailed Description, given by way of example, but not intended to limit the invention to specific embodiments described, may be understood in conjunction with the accompanying drawings, incorporated herein by reference. Various preferred features and embodiments of the present invention will now be described by way of non-limiting example and with reference to the accompanying drawings, in which:

Figure 1 is a schematic showing chemotaxis, chemokinesis, and fugetaxis in a T cell migration assay.

Figures 2A and 2B are schematics showing putative downstream events that result following chemokine engagement at the cell surface.

Figures 3 through 8 indicate the genes that are significantly (p value $\leq$ to 0.05; fold change $\geq$ 1.7) differentially regulated under different gradient conditions of SDF-1. Gen Bank Accession Numbers are provided to further describe the identified gene products.

Figure 3 depicts Table 1, indicating genes that are differentially regulated in Medium vs. Chemokinesis gradients of SDF-1. Positive values are upregulated in Chemokinesis; Negative values are down regulated in Chemokinesis; $p \leq 0.05$.

Figure 4 depicts Table 2, indicating genes that are differentially regulated in Fugetaxis vs. Chemotaxis gradients of SDF-1. Positive values are upregulated in Fugetaxis; Negative values are up regulated in Chemotaxis; $p \leq 0.05$.

Figure 5 depicts Table 3, indicating genes that are differentially regulated in Chemokinesis vs. Chemotaxis gradients of SDF-1. Positive values are upregulated in Chemotaxis; Negative values are downregulated in Chemotaxis; $p \leq 0.05$.

Figure 6 depicts Table 4, indicating genes that are differentially regulated in Chemokinesis vs. Fugetaxis gradients of SDF-1. Positive values are upregulated in Fugetaxis; Negative values are downregulated in Fugetaxis; $p \leq 0.05$.

Figure 7 depicts Table 5, indicating genes that are differentially regulated in Medium vs. Chemotaxis gradients of SDF-1. Positive values are upregulated in Chemotaxis; Negative values are downregulated in Chemotaxis; $p \leq 0.05$.

Figure 8 depicts Table 6, indicating genes that are differentially regulated in Medium vs. Fugetaxis gradients of SDF-1. Positive values are upregulated in Chemotaxis; Negative values are downregulated in Chemotaxis; $p \leq 0.05$.

Figure 9 depicts Table 7, indicating actin/cytoskeletal, extracellular matrix/adhesion, T-cell activation and migration related proteins differentially regulated under different gradient conditions of SDF-1.

Figures 10A through 10P depict the migration of human neutrophils in a continuous (0, 12nm, 120nM or 1.2 mM) linear gradient of IL-8 in microfabricated devices. Cell migration in uniform concentrations or continuous gradients of IL-8 (tracked with the assistance of MetaMorph software) is depicted in Figures 10E

through 10H. Normalized cell concentration across the migration channel (measured by MetaMorph software) is depicted in Figures 10I through L. Distribution of movement vector angles for all cells for all time points is depicted in Figures 10M through P.

Figures 11A and 11B depict lots of mean speeds (11A) and mean square displacement (11B) for cells tracked over time in videos of cells migrating in the absence of IL-8 or defined as continuous linear gradients of the chemokine at peak concentrations of 12nM, 120nM and 1.2 mM.

Figure 12 depicts effect of SB225002 on directional migration of neutrophils towards and away from IL-8.

Figure 13 depict effects of chemokine signal transduction pathway inhibitors on directional human neutrophil migration in defined continuous gradients of IL-8.

Figures 14A through 14I depict intravital microscopic quantitation of rat neutrophil migration in response to continuous diffusive gradients of the IL-8 orthologue, CINC-1. Diffusive continuous gradients are mathematically modeled and depicted in Figures 14A, 14B and 14C. A single photomicrograph derived from the first frame of the timelapse video is depicted in 14D(Video 5), 14E(Video 6) and 14F(Video 7). Figures 14G, 14H and 14I depict cell tracks normalized to an origin and again use the same color code as in Figure 14 for directional and random cell movement.

Figure 15 depicts quantitative parameters defined for measuring the directional bias and orientation of cellular movement of cells tracked in videos of neutrophils migrating in the absence of IL-8 (No-IL-8), a constant concentration of chemokine (120nM IL-8 no gradient), and three continuous linear gradient conditions with peak concentrations of IL-8, 12nM, 120nM and 1.2mM within microfabricated devices (Table 8).

Figure 16 depicts quantitated motility parameters for rat neutrophils migrating in response to diffusive continuous CINC-1 gradients *in vivo* (Table 9).

DETAILED DESCRIPTION OF THE INVENTION

The invention is premised in part on the discovery that cells exposed to a gradient undergo gene expression changes associated with the presence of the gradient and movement through the gradient. It has been unexpectedly found that

exposure of cells to an agent gradient causes differential gene expression in cells so exposed as compared to cells exposed to a uniform agent concentration (i.e., no gradient). As a result, gene expression profiles during or following exposure to gradients is significantly different from those observed during or following exposure to uniform agent concentrations. Furthermore, gene expression profiles are dependent on the structure of the gradient. That is, if the gradient is oriented such that the cell is attracted to an agent source (an attractant gradient or a chemoattractant agent), the gene expression profile will be different than if the gradient is oriented such that the cell is repelled from the agent source (a fugetactic gradient or agent). Gene expression profiles for cells exposed to a fugetactic gradient are clearly distinct from those seen in chemotactic gradients. As an example, when a cell is exposed to an SDF-1 (CXCL12) gradient, it begins to differentially express genes involved in chemokine signal transduction depending upon whether it is migrating towards or away from an agent source.

Definitions

As used in accordance with terms appearing herein, the following definitions are provided:

An "agent" is a diffusible substance that can alter gene expression in a migratory cell, either alone or in combination with other agents. Preferably, the agent is an attractant or repellant of a migratory cell.

An "agent concentration gradient" is a gradually increasing concentration of an agent, wherein the location of highest agent concentration is at the agent source.

A "continuous gradient" is a physiologically relevant, continuous agent concentration range over a fixed distance.

A "step gradient" comprises agent concentrations that descend or ascend abruptly to another concentration of the agent.

An "agent source" is the point at which the concentration of an agent is highest. As a cell migrates towards the source, it is moving towards higher agent concentration, and as it migrates away from the source, it is moving towards lower agent concentration.

A "ligand" is a molecule, such as a protein, lipid or cation, capable of binding to another molecule for which it has affinity, such as a receptor. A ligand is therefore one member of a binding interaction or association.

"Chemotactic migration" or "chemotaxis" is the movement of a migratory cell toward an agent source (i.e., towards a higher concentration of agent).

"Fugetactic migration" or "fugetaxis" is the movement of a migratory cell away from an agent source (i.e., towards a lower concentration of agent).

"Chemokinetic migration" or "chemokinesis" is the random movement of cells irrespective of a gradient.

A "cytokine" is generic term for all extracellular proteins or peptides that mediate cell-cell communication, often with the effect of altering the activation state of cells.

A "chemokine" is a cytokine with a conserved cysteine motif and which can serve as an attractant.

A "signaling molecule" is a molecule involved in the transduction of a signal cascade from one compartment of the cell to another (e.g., in the case of cell movement, a signaling molecule can be involved in the transduction of a signal cascade from the cell membrane to the actin cytoskeleton).

A "cytoskeleton related molecule" is a component of the cytoskeleton, which is a system of protein filaments (e.g., actin filaments, integrins, microtubules and intermediate filaments) in the cytoplasm of a eukaryotic cell that gives the shape and capacity for cellular movement.

A "cell cycle molecule" is a molecule involved in regulating, initiating or halting the reproductive cycle of a cell, which is the cycle by which a cell duplicates its contents and divides into two.

An "extracellular matrix related molecule" is a molecule that is a component of the extracellular matrix, which is a network of structural elements, such as polysacchrides and proteins, secreted by cells.

An "immune response related molecule" is a molecule involved in the generation, propagation or termination of an immune response, which is a response by an immune cell to an antigen.

An "immune cell" is a cell of hematopoietic origin that is involved in the specific recognition of antigens. Immune cells include, but are not limited to T-cells, B-cells, NK cells, dendritic cells. monocytes and macrophages.

"Primary cells" are cells directly obtained from living normal or diseased tissues.

An "inflammatory cell" is a cell contributing to an immune response including, but not limited to, neutrophils, basophils, eosinophils and mast cells.

Additional definitions and descriptions appear in context below.

Other aspects of the invention are disclosed in, or are obvious from the following disclosure and are within the ambit of the invention.

Methods of the Invention

The methods of the invention can be used to determine the differences between cells that undergo chemotaxis versus those that undergo fugetaxis, or differences between cells that undergo either chemotaxis or fugetaxis versus those that undergo chemokinesis (i.e., random movement). In some instances, gene expression profiles of cells undergoing chemokinesis are considered "background" and thus subtracted from both chemotactic and fugetactic gene expression profiles.

These expression differences identify further mediators of chemotaxis and fugetaxis and provide novel targets that can be affected in order to modulate directed cell movement. In some instances, these newly identified targets can be administered to cells directly. Alternatively, the newly identified targets can be up-regulated or down-regulated in ways that are independent of actual exposure to a chemotactic or fugetactic gradient. These include introduction of nucleic acids into cells (e.g., antisense or gene therapy), and exposure of cells to compounds that modulate the newly identified targets (e.g., agonists or antagonists).

Yet another unexpected finding of the invention is the observation that cells are capable of sensing not only differences in agent concentration, but also differences in agent concentration along their length. Previous work relating to concentration gradients and cells compared cells in differing concentrations. The invention is based in part on the finding that cells respond to changes in concentration, but also are able to sense their position in a gradient based on the difference in agent concentration along the length of the cell. That is, a cell can sense its position in a gradient, and thereby modulate its expression profile, by sensing that its opposite ends are exposed to different agent concentrations.

In one aspect, the invention provides a method for identifying a nucleic acid expressed in an agent concentration dependent manner. The method comprises determining a first nucleic acid expression profile of a first cell at a first position in an agent concentration gradient, determining a second nucleic acid expression

profile of a second cell at a second position in the agent concentration gradient, and determining a difference between the first and second nucleic acid expression profiles, wherein the first position in the agent concentration gradient corresponds to a first concentration of agent, and the second position in the agent concentration gradient corresponds to a second concentration of agent.

In some embodiments, at least the second cell has migrated through the agent concentration gradient. Therefore, the invention provides a method for identifying a nucleic acid expressed in a concentration dependent manner, comprising determining a first nucleic acid expression profile of a first cell at a first position in an agent concentration gradient, determining a second nucleic acid expression profile of a second cell that has migrated through the agent concentration gradient, and determining a difference between the first and second nucleic acid expression profiles.

In another embodiment, the second cell is positioned in the gradient such that a gradient exists along the length (or diameter) of the cell. In other words, the agent concentration at one end of the cell (e.g., the leading edge of the cell) is different that the agent concentration at the opposite end of the cell (e.g., the lagging edge of the cell). Thus, the method may be performed by placing a cell into a preformed concentration gradient, or allowing the cell to move through the concentration gradient, depending upon the application and information desired.

The chemotactic, fugetactic or chemokinetic response can be measured as described herein, or according to the transmigration assays described in greater detail in U.S. Patent US 6,448,054 B1, and in U.S. Patent 5,514,555, entitled: "Assays and therapeutic methods based on lymphocyte chemoattractants," issued May 7, 1996, to Springer, TA, et al.). Other suitable methods will be known to one of ordinary skill in the art and can be employed using only routine experimentation.

Agent concentration gradients can be established using an agent source. The agent source is the location in a gradient having the highest concentration of agent, and is generally the location at which agent is supplied to establish the gradient. Agent can be continually supplied or the source can be over-saturated with agent that there is no need for replenishment of the agent during the course of the screening. In preferred embodiments, the gradient is established and it remains constant throughout the screening process. That is, the concentration differential

between the agent source and the end of the gradient is constant, as is the concentration differential between different locations in the gradient.

In some embodiments, the first concentration of agent is a zero concentration of agent, and the second concentration of agent is a non-zero concentration of agent, while in other embodiments the first concentration of agent is greater than the second concentration of agent. The cells might migrate through the gradient, and in these embodiments, one or both cells will migrate through the agent concentration gradient. The migration may be fugetactic migration, or chemotactic migration. The gradient can be either a step gradient or a continuous gradient, although a continuous gradient is preferred in some embodiments. In still another embodiment, there may be a second gradient overlapped onto the first gradient. In an important embodiment, the first cell has undergone chemotaxis and the second cell has undergone fugetaxis, and the expression profiles of these cells are compared.

The nucleic acid expression profile can be an RNA (preferably an mRNA) profile or it can be a protein profile. Depending upon which expression product is being analysed, the method of analysis and quantitation of the expression product will differ. If the nucleic acid expression product is itself a nucleic acid, such as an RNA (e.g., mRNA), then it can be quantitated using a number of methods including but not limited to Northern analysis, reverse-transcriptase polymerase chain reaction (RT-PCR), subtractive hybridization, differential display, representational difference analysis and cDNA microarray analysis. In some embodiments, the nucleic acids are harvested from the cells and analyzed without the need for in vitro amplification.

The differentially expressed molecule can be identified in a number of ways. If the expression product is a nucleic acid (i.e., an mRNA), then it may be identified using techniques such as subtractive hybridization (including suppression subtractive hybridization), differential display, representational difference analysis, or microarray analysis (e.g., Affymetrix chip analysis). These techniques have been reported in the literature, and thus one of ordinary skill will be familiar with these. (See, for example, Methods Enzymol 303:349-380, 1999; Ying and Lin in Biotechniques 26:966-8, 1999; Zhao et al., J Biotechnol 73:35-41, 1999; and Blumberg and Belmonte in Methods Mol Biol 97:555-574, 1999.) Sequences isolated in this screening process can then be sequenced and compared to the GenBank non-redundant and EST databases using the BLAST algorithm.

Another important technique for identifying differentially expressed transcripts involves DNA chip technology and cDNA microarray hybridization. This technique is able to analyze hundreds if not thousands of coding sequences at a time. Standard and custom-made DNA chips are now commercially available from manufacturers such as Affymetrix and InCyte. These approaches have evolved to the extent that high throughput screening for difference sequences can be readily accomplished. (Von Stein, et al., Nucleic Acids Res 25:2598-602, 1997; Carulli, et al., J Cell Biochem Suppl 30-31:286-96, 1998) One of the major advantages of DNA chip technology is that no RNA amplification is required.

If the nucleic acid expression product is a protein, then it may be identified using, for example, gel electrophoresis separation followed by Coomassie Blue staining. In this latter approach, differences between the experimental cell and a control may be revealed by the presence or absence of stained protein bands. Further separation, sequencing and cloning of these "difference bands" would then be required, all of which are within the realm of the ordinary artisan. Other approaches can similarly be used to identify and/or quantitate nucleic acid expression products that are proteins, and these include but are not limited to immunohistochemistry, Western analysis, and fluorescence activated cytometry.

The agent to be used in establishing a gradient is not intended to be limiting. Any agent that induces a change in gene expression profile would be suitable. The agent can be a ligand, resulting in a ligand concentration gradient. Accordingly, the ligand can also be a receptor. In some preferred embodiments, the agent is a molecule that induces chemotaxis or fugetaxis.

The agent may be a cytokine (including a chemokine). For a further description of a cytokine, see Human Cytokines: Handbook for Basic & Clinical Research (Aggrawal, et al. eds., Blackwell Scientific, Boston, Mass. 1991) (which is hereby incorporated by reference in its entirety for all purposes). Examples of cytokines include PAF, N-formylated peptides, C5a, LTB_4 and LXA_4, chemokines: CXC, IL-8, GCP-2, GRO, GROα, GROβ, GROγ, ENA-78, NAP-2, IP-10, MIG, I-TAC, SDF-1α, BCA-1, PF4, Bolekine, MIP-1α, MIP-1β, RANTES, HCC-1, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5 (mouse), Leukotactin-1 (HCC-2, MIP-5), Eotaxin, Eotaxin-2 (MPIF2), Eotaxin-3 (TSC), MDC, TARC, SLC (Exodus-2, 6CKine), MIP-3α (LARC, Exodus-1), ELC (MIP-3β), I-309, DC-CK1 (PARC,

AMAC-1), TECK, CTAK, MPIF1 (MIP-3), MIP-5 (HCC-2), HCC-4 (NCC-4), MIP-1γ (mouse), C-10 (mouse), C Lymphotactin, and CX_3C Fracktelkine (Neurotactin). The cytokine can be a member of the Cys-X-Cys family of chemokines (e.g., chemokines that bind to the CXCR-4 receptor). Preferred cytokines of the invention include SDF-1α, SDF-1β, met-SDF-1β, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-10, IL-12, IL-15, IL-18, TNF, IFN-α, IFN-β, IFN-γ, granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), macrophage colony stimulating factor (M-CSF), TGF-β, FLT-3 ligand, VEGF, DMDA, endothelin, and CD40 ligand. This list is not meant to be exhaustive and one of ordinary skill will be able to identify other cytokines that can be used in the methods of the invention. In certain embodiments, the cytokine is a cytokine with chemoattractant and/or chemokinetic properties.

The agent may be a chemokine. Chemokines, or chemoattractant cytokines, are a family of small proteins with a conserved cysteine motifs. These small proteins have been implicated in a wide range of disease states, such as acute and chronic inflammatory processes, angiogenesis, leukocyte migration, regulation of cell proliferation and maturation, hematopoiesis, viral replication, and other immunoregulatory functions. Chemokines are expressed by a number of different cells and have distinct but overlapping cellular targets.

Chemokines have been classified into four subgroups, depending on the nature of the spacing of two highly-conserved cysteine amino acids that are located near the amino terminus of the polypeptide. The first chemokine subgroup is referred to as "CXC"; the second subgroup is referred to as "CC"; the third chemokine subgroup is referred to as "CX3C"; and the fourth chemokine subgroup is referred to as "C". Within these subgroups, the chemokines are further divided into related families that are based upon amino acid sequence homology. The CXC chemokine families include the IP-10 and MIG family; the GROα, GROβ, and GROβ family; the interleukin-8 (IL-8) family; and the PF4 family. The CC chemokine families include the monocyte chemoattractant protein (MCP) family; the family including macrophage inhibitory protein-1α (MIP-1α), macrophage inhibitory protein-1β (MIP-1β), and regulated on activation normal T cell expressed (RANTES). The stromal cell-derived factor 1α (SDF-1α) and stromal cell-derived factor 1β (SDF-1β) represent a chemokine family that is approximately equally

related by amino acid sequence homology to the CXC and CC chemokine subgroups. The CX3C chemokine family includes fractalkine; the C chemokine family includes lymphotactin.

In general, the CXC chemokines are bound by members of the CXCR class of receptors; the CC chemokines are bound by the CCR class of receptors; the CX3C chemokines are bound by the CX3CR class of receptors; and the C chemokines are bound by the CR class of receptors. The majority of chemokine receptors are transmembrane spanning molecules which belong to the family of G-protein-coupled receptors. Many of these receptors couple to guanine nucleotide binding proteins to transmit cellular signals.

Chemokines and receptor expression is upregulated during inflammatory responses and cellular activation. Chemokines, through binding to their respective receptors, have been shown to be involved in a number of physiologic conditions. For instance, chemokines of the CXC group, like interleukin-8, can stimulate angiogenesis, while platelet factor-4, growth-related oncogene-β (GRO-β) and interferon-γ induced protein-10 (IP-10) inhibit endothelial cell proliferation and angiogenesis. Interleuken-8 stimulates endothelial cell proliferation and chemotaxis in vitro, and appears to be a primary inducer of macrophage induced angiogenesis. It was shown that the activities of these chemokines are dependent on the NH_2-terminal amino acid sequence (Streiter et al., J. Biol. Chem., 270:27348-27357). SDF-1, another CXC chemokine, is active in the recruitment and mobilization of hematopoietic cells from the bone marrow, as well as the attraction of monocytes and lymphocytes.

The agent can be any molecule, either naturally occurring or synthetically produced. The agent may be isolated from a biological sample such as a biological fluid. Biological fluids include but are not limited to synovial fluid, cerebral spinal fluid, fallopian tube fluid, seminal fluid, ocular fluid, pericardial fluid, pleural fluid, inflammatory exudate, and ascitic fluid. The agent may also be present in a tumor cell culture supernatant, tumor cell eluate and/or tumor cell lysate.

In preferred embodiments, the agent is a molecule that induces chemotaxis or fugetaxis. In another embodiment, the agent is a fugetactic agent at one concentration and a chemotactic agent at a lower concentration.

The cells to be used in the methods of the invention are not limited to cell type, provided it has migratory capacity. An example of a cell with migratory capacity is a hematopoietic cell, such as neutrophils, basophils, eosinophils, monocytes, macrophages, dendritic cells, T cells, and the like. In some embodiments, the cell with migratory capacity is a neural cell. In further embodiments, the cell with migratory capacity is an epithelial cell. In yet further embodiments, the cell with migratory capacity is a mesenchymal cell. In some embodiments, the cell with migratory capacity is an embryonic stem cell. In certain embodiments, the cell with migratory capacity is a germ cell. In important embodiments, the cells are mammalian cells, such as human cells. In important embodiments, the cells are primary human T cells. In other embodiments, the cells are neural cells such as neurons capable of undergoing chemotaxis or fugetaxis for example in response to a neurotransmitter.

Cells which express chemokine receptors include migratory cells such as lymphocytes, granulocytes, and antigen-presenting cells (APCs) that are believed to participate in immune responses or that may release other factors to mediate other cellular processes in vivo. The presence of a chemokine gradient serves to attract migratory cells which express the chemokine receptors. For example, migratory cells can be attracted by a chemokine gradient to a particular site of inflammation, at which location they play a role in further modifying the immune response.

"Immune cells" as used herein are cells of hematopoietic origin that are involved in the specific recognition of antigens. Immune cells include antigen presenting cells (APCs), such as dendritic cells or macrophages, B cells, T cells, etc. "Mature T cells" as used herein include T cells of a $CD4^{lo}CD8^{hi}CD69^{+}TCR^{+}$, $CD4^{hi}CD8^{lo}CD69^{+}TCR^{+}$, $CD4^{+}CD45^{+}RA^{+}$, $CD4^{+}CD3^{+}RO^{+}$, and/or $CD8^{+}CD3^{+}RO^{+}$ phenotype. Fugetaxis may play a role in the emigration of T cells from the thymus during development.

Cells of "hematopoietic origin" include, but are not limited to, pluripotent stem cells, multipotent progenitor cells and/or progenitor cells committed to specific hematopoietic lineages. The progenitor cells committed to specific hematopoietic lineages may be of T cell lineage, B cell lineage, dendritic cell lineage, Langerhans cell lineage and/or lymphoid tissue-specific macrophage cell lineage. The hematopoietic cells may be derived from a tissue such as bone marrow, peripheral

blood (including mobilized peripheral blood), umbilical cord blood, placental blood, fetal liver, embryonic cells (including embryonic stem cells), aortal-gonadal-mesonephros derived cells, and lymphoid soft tissue. Lymphoid soft tissue includes the thymus, spleen, liver, lymph node, skin, tonsil and Peyer's patches. In other embodiments, the "hematopoietic origin" cells may be derived from in vitro cultures of any of the foregoing cells, and in particular in vitro cultures of progenitor cells.

Cells of neural origin, include neurons and glia, and/or cells of both central and peripheral nervous tissue that express RR/B (see, U.S. Patent 5,863,744, entitled: "Neural cell protein marker RR/B and DNA encoding same," issued January 26, 1999, to Avraham, et al.). Work in Xenopus indicates that neurons and growth cones respond to netrins. Neurons are expected to respond either by chemotaxing or fugetaxing to the presence of neurotransmitters. Cells of epithelial origin, include cells of a tissue that covers and lines the free surfaces of the body. Such epithelial tissue includes cells of the skin and sensory organs, as well as the specialized cells lining the blood vessels, gastrointestinal tract, air passages, ducts of the kidneys and endocrine organs. Cells of mesenchymal origin include cells that express typical fibroblast markers such as collagen, vimentin and fibronectin. Cells involved in angiogenesis are cells that are involved in blood vessel formation and include cells of epithelial origin and cells of mesenchymal origin. An embryonic stem cell is a cell that can give rise to cells of all lineages; it also has the capacity to self-renew. A germ cell is a cell specialised to produce haploid gametes. It is a cell further differentiated than a stem cell that can still give rise to more differentiated germ-line cells. The cell may be a eukaryotic cell or a prokaryotic cell.

In some embodiments, the cells used in the screening assays are adult cells. Preferably, they are human cells. They may be primary cells (e.g., directly harvested cells), or they may be secondary cells (including cells from a cell line).

The invention in one aspect identifies differential expression products that are upregulated or downregulated during chemokinesis (i.e., random movement), as compared to cells in medium alone. The identification of these products can be exploited in instances where it is desired to inhibit or facilitate cell movement. Products upregulated during chemokinesis include the signaling molecules PTK2 (focal adhesion kinase) (upregulated by a value of 6.88) and regulator of G-protein signaling 10 (upregulated by a value of 2.53). Products downregulated during

chemokinesis include the signaling molecules phospholipase C beta 3 (downregulated by a value of 2.54), RAS p21 protein activator (GAP) 3 (downregulated by a value of 2.20), RAS guanyl releasing protein 2 (calcium/DAG) (downregulated by a value of 2.16), G protein-coupled receptor kinase 6 (downregulated by a value of 2.15), Rho-specific GEF (p114) (downregulated by a value of 1.70) and protein kinase C substrate 80K-H (downregulated by a value of 1.70). Knowledge of these products at a minimum allows for the identification of products that are specifically differentially regulated in response to either chemotaxis or fugetaxis (i.e., it is possible to distinguish between those products that are impacted by purposeful directional movement rather than simply random movement). The data provided in the tables below are generally presented as levels of expression of a particular gene product relative to the level of that gene product when the cell from which it is derived is placed in medium alone or is allowed to undergo chemokinesis. Knowledge of these products also leads to methods for inhibiting or stimulating movement of cells, depending upon the desired effect. It is possible that many of these products are required in chemotaxis and fugetaxis and thus provide another target for preventing or stimulating these directional migrations. In this way, these "chemokinesis" specific products can be thought of as the "housekeeping products" of cell movement in general (i.e., they are required for movement, regardless of whether the movement is directional or not). Agents that stimulate these products include agonists and nucleic acids that encode the products, but are not so limited. Agents that inhibit these products include antagonists, antibodies, and antisense nucleic acids, but are not so limited.

In another aspect, the invention provides a method for identifying a compound that can modulate cell migration in one or more agent concentration gradients comprising contacting a migratory cell in an agent concentration gradient with a test compound, determining the nucleic acid expression profile in the cell and identifying a change in expression of a gene expression product. Cell movement can be chemotaxis or fugetaxis and therefore, the gene expression product can be a chemotaxis or fugetaxis specific gene product. A test compound is any compound that is thought to potentially modulate chemotaxis or fugetaxis.

The invention further provides methods of modulating chemotaxis and fugetaxis. As used herein, modulate means to affect or change, and includes

stimulation or inhibition. In order to modulate chemotaxis or fugetaxis, cells are contacted or exposed to agents that are differential expression products as identified according to the invention, or that impact upon the differential expression products. The differential expression products identified according to the invention are thus additional, previously unrecognized targets that can be manipulated in order to modulate chemotaxis or fugetaxis.

The ability to modulate chemotaxis and fugetaxis is important for manipulating bodily processes, such as but not limited to immune responses, thymic emigration, and neural outgrowth (for example, in response to neurotransmitters). In some instances, it will be desirable to inhibit an immune response that is occurring or is likely to occur in a subject. Examples include subjects that have asthma, allergy, autoimmune diseases such as rheumatoid arthritis, infections that are detrimental due to the immune response that is formed in response (e.g., RSV infection, particularly in infants), inflammatory conditions, graft versus host disease (GVHD), and the like. In other instances, it will be desirable to promote or stimulate an immune response where a subject is likely to benefit from such a response. These subjects include those that have or are likely to develop infections (e.g., bacterial infections, viral infections, fungal infection, parasitic infections), and those that have or are likely to develop a cancer in order to heighten immune surveillance for cancer cells. Other subjects include those that are diagnosed as having an impaired immune response, particularly where the defect lies in the inability of immune cells to respond to chemotactic factors.

Accordingly, in one embodiment, a cell undergoing or likely to undergo fugetaxis is contacted or exposed to an agent that inhibits a fugetaxis specific gene expression product in an amount effective to inhibit fugetaxis. The fugetaxis inhibiting agent can act at the nucleic acid or protein level. Fugetaxis specific gene expression products are those that are upregulated in response to fugetaxis as compared to their level when the cells are moving randomly (i.e., chemokinesis) or when the cells are chemotaxing. Since these products are upregulated in response to fugetaxis, fugetaxis may be inhibited by blocking the activity of these products using a number of methods known in the art, including but not limited to antisense and antibody approaches. The products can also be targeted in order to modulate chemotaxis, as one of ordinary skill will understand.

The signaling molecules can be but are not limited to cell division cycle 42, annexin A3, Rap1 guanine nucleotide exchange factor, adenylate cyclase 1, JAK binding protein, and Rho GDP dissociation inhibitor alpha. In another embodiment, the signaling molecule is cell division cycle 42 (cdc42), ribosomal protein S6 kinase, BAI1-associated protein 2, GTPase regulator associated with FAK, protein kinase C-beta 1, phosphoinositide-specific phospholipase C-beta 1, nitric oxide synthase 1, phosphatidylinositol-4-phosphate 5-kinase, and MAP kinase kinase kinase kinase 4.

The extracellular matrix related molecules can be but are not limited to Chitinase 3-like 1 (cartilage glycoprotein-39), carcinoembryonic antigen-related cell adhesion molecule 6, matrix metalloproteinase 8 (neutrophil collagenase), integrin cytoplasmic domain-associated protein 1, ficolin (collagenfibrinogen domain-containing) 1, epithelial V-like antigen 1, vascular endothelial growth factor (VEGF), fibulin 1, carcinoembryonic antigen-related cell adhesion molecule 3, and lysosomal-associated membrane protein 1.

The cytoskeleton related molecules can be but are not limited to Ankyrin 1 (erythrocytic), S100 calcium-binding protein A12 (calgranulin C), plectin 1 (intermediate filament binding protein, 500kD), microtubule-associated protein RPEB3, microtubule-associated protein 1A like protein (MILP), capping protein (actin filament, gelsolin-like), and ankyrin 2 (neuronal).

The cell cycle molecules can be but are not limited to V-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog, lipocalin 2 (oncogene 24p3), lectin, (galactoside-binding, galectin 3), RAB31 (member RAS oncogene family), disabled (Drosophila) homolog 2 (mitogen-responsive phosphoprotein), RAB9 (member RAS oncogene family, pseudogene 1), and growth differentiation factor 8.

The immune response related molecules can be but are not limited to major histocompatibility complex (class II, DR alpha), S100 calcium-binding protein A8 (calgranulin A), small inducible cytokine subfamily A (Cys-Cys), eukaryotic translation initiation factor 5A, small inducible cytokine subfamily B (Cys-X-Cys) (member 6, granulocyte chemotactic protein 2), Fc fragment of IgG binding protein, CD24 antigen (small cell lung carcinoma cluster 4 antigen), cytochrome P450 (subfamily IVF, polypeptide 3, leukotriene B4 omega hydroxylase), MHC class II transactivator, T cell receptor (alpha chain), T cell activation (increased late

expression), MKP-1 like protein tyrosine phosphatase, T cell receptor gamma constant 2, T cell receptor gamma locus.

The fugetaxis specific gene expression product may also be chemokine (C-X3-C) receptor 1.

The invention further provides a method for inhibiting cell chemotaxis. The method involves contacting a cell undergoing or likely to undergo chemotaxis with an agent that inhibits a chemotaxis specific gene expression product in an amount effective to inhibit chemotaxis.

The chemotaxis inhibiting agent can act at the nucleic acid or protein level. Chemotaxis specific gene expression products are those that are upregulated in response to chemotaxis as compared to their level in chemokinesis or in fugetaxis. Since these products are upregulated in response to chemotaxis, chemotaxis may be inhibited by blocking the activity of these products using a number of methods known in the art, including but not limited to antisense and antibody approaches.

The signaling molecules can be but are not limited to G protein-coupled receptor kinase 6, vaccinia related kinase 1, PTK2 protein tyrosine kinase 2, STAM-like protein containing SH3 and ITAM domains 2, signal-induced proliferation-associated gene 1, CD47 antigen (Rh-related antigen, integrin-associated signal transducer), and protein tyrosine phosphatase (non-receptor type 12). The signaling molecule may also be selected from the group consisting of PTK2 (focal adhesion kinase), MAP kinase kinase kinase kinase 2, guanine nucleotide binding protein, PT phosphatase (receptor), cdc42-binding protein kinase beta, Ral GEF (RalGPS1A), MAP kinase 7, autotaxin, inositol 1,4,5-triphosphate receptor, phosphoinositide-3-kinase gamma, PT phosphatase (non-receptor), RAS p21 protein activator (GAP), RAS guanyl releasing protein 2, and Arp23 complex 20kDa subunit.

The extracellular matrix related molecules can be but are not limited to spondin 1 (f-spondin, extracellular matrix protein), collagen type XVIII (alpha 1), CD31 adhesion molecule, tetraspan 3, glycoprotein A33, and angio-associated migratory cell protein.

The cytoskeleton related molecules can be but are not limited to actin related protein 23 complex (subunit 4, 20 kD), tropomyosin 2 (beta), SWISNF related matrix associated actin dependent regulator of chromatin (subfamily a, member 5),

spetrin beta (non-erythrocytic 1), myosin (light polypeptide 5, regulatory), keratin 1, plakophilin 4, and capping protein (actin filament, muscle Z-line, alpha 2).

The cell cycle molecules can be but are not limited to FGF receptor activating protein 1, v-maf musculoaponeurotic fibrosarcoma (avian) oncogene homolog, cyclin-dependent kinase (CDC2-like) 10, TGFB inducible early growth response 2, retinoic acid receptor alpha, anaphase promoting complex subunit 10, RAS p21 protein activator (GTPase activating protein, 3-Ins-1,3,4,5, -P4 binding protein), cell division cycle 27, programmed cell death 2, c-myc binding protein, mitogen-activated protein kinase kinase kinase 1, TGF beta receptor III (betaglycan, 300 kDa), and G1 to S phase transition 1.

The immune response related molecules can be but are not limited to major histocompatibility complex class II DQ beta 1, bone marrow stromal cell antigen 2, Burkitt lymphoma receptor 1 (GTP binding protein, CXCR5), CD7 antigen (p41), Stat2 type a, T cell immune regulator 1, and interleukin 21 receptor.

The contacting of cells with the inhibitory or stimulatory agents of the invention can occur in vivo. And as mentioned above the subject receiving the agent will vary depending upon the type of agent being administered. Thus, in one embodiment where the method is intended to inhibit chemotaxis, the subject is one having or at risk of having an abnormal immune response.

The abnormal immune response may be an inflammatory response or an autoimmune response but it is not so limited. Autoimmune disease is a class of diseases in which an subject's own antibodies react with host tissue or in which immune effector T cells are autoreactive to endogenous self peptides and cause destruction of tissue. Autoimmune diseases include but are not limited to rheumatoid arthritis, Crohn's disease, multiple sclerosis, systemic lupus erythematosus (SLE), autoimmune encephalomyelitis, myasthenia gravis (MG), Hashimoto's thyroiditis, Goodpasture's syndrome, pemphigus (e.g., pemphigus vulgaris), Grave's disease, autoimmune hemolytic anemia, autoimmune thrombocytopenic purpura, scleroderma with anti-collagen antibodies, mixed connective tissue disease, polymyositis, pernicious anemia, idiopathic Addison's disease, autoimmune-associated infertility, glomerulonephritis (e.g., crescentic glomerulonephritis, proliferative glomerulonephritis), bullous pemphigoid,

Sjögren's syndrome, insulin resistance, insulin-dependent diabetes mellitus, uveitis, rheumatic fever, Guillain-Barre syndrome, psoriasis, and autoimmune hepatitis.

According to still another aspect of the invention, a method is provided for promoting fugetaxis. The method involves contacting a cell with a non-chemokine agent that promotes fugetaxis in an amount effective to promote fugetaxis. In one embodiment, the contacting occurs in vivo in a subject having a disorder characterized by abnormal fugetaxis. As used herein, a non-chemokine agent is an agent that is not a chemokine such as those recited above. The non-chemokine agent is preferably one of the downstream targets of fugetaxis identified according to the invention, or it is an agonist thereof.

The invention further provides a method for promoting chemotaxis. The method involves contacting a cell with a non-chemokine agent that promotes chemotaxis in an amount effective to promote chemotaxis. In one embodiment, the contacting occurs in vivo in a subject having a disorder characterized by lack of chemotaxis. The non-chemokine agent is preferably one of the downstream targets of fugetaxis identified according to the invention, or it is an agonist thereof.

As stated above, in some instances, modulating occurs by administration of nucleic acids (e.g., in antisense therapy), or proteins or peptides (e.g., antibody therapy). In some embodiments, the nucleic acids or proteins/peptides are isolated. In still further embodiments, the nucleic acids or proteins/peptides are substantially pure.

As used herein with respect to nucleic acids, the term "isolated" means: (i) amplified in vitro by, for example, polymerase chain reaction (PCR); (ii) recombinantly produced by cloning; (iii) purified, as by cleavage and gel separation; or (iv) synthesized by, for example, chemical synthesis. An isolated nucleic acid is one which is readily manipulable by recombinant DNA techniques well known in the art. Thus, a nucleotide sequence contained in a vector in which 5' and 3' restriction sites are known or for which polymerase chain reaction (PCR) primer sequences have been disclosed is considered isolated but a nucleic acid sequence existing in its native state in its natural host is not. An isolated nucleic acid may be substantially purified, but need not be. For example, a nucleic acid that is isolated within a cloning or expression vector is not pure in that it may comprise only a tiny percentage of the material in the cell in which it resides. Such a nucleic acid is

isolated, however, as the term is used herein because it is readily manipulable by standard techniques known to those of ordinary skill in the art.

As used herein with respect to proteins/peptides, the term "isolated" means separated from its native environment in sufficiently pure form so that it can be manipulated or used for any one of the purposes of the invention. Thus, isolated means sufficiently pure to be used (i) to raise and/or isolate antibodies, (ii) as a reagent in an assay, or (iii) for sequencing, etc.

The term "substantially pure" means that the nucleic acid or protein/peptide is essentially free of other substances with which it may be found in nature or in vitro systems, to an extent practical and appropriate for their intended use. Substantially pure polypeptides may be produced by techniques well known in the art. As an example, because an isolated protein may be admixed with a pharmaceutically acceptable carrier in a pharmaceutical preparation, the protein may comprise only a small percentage by weight of the preparation. The protein is nonetheless isolated in that it has been separated from many of the substances with which it may be associated in living systems, i.e. isolated from certain other proteins.

According to another aspect, the invention provides compositions and methods relating to attracting or repelling immune cells to or from a material surface. These aspects of the invention involve coating or loading material surfaces alternatively with the chemotactic inhibiting agents, the chemotactic stimulating agents, the fugetactic inhibiting agents, or the fugetactic stimulating agents provided herein. "Material surfaces" as used herein, include, but are not limited to, dental and orthopedic prosthetic implants, artificial valves, and organic implantable tissue such as a stent, allogeneic and/or xenogeneic tissue, organ and/or vasculature.

Implantable prosthetic devices have been used in the surgical repair or replacement of internal tissue for many years. Orthopedic implants include a wide variety of devices, each suited to fulfill particular medical needs. Examples of such devices are hip joint replacement devices, knee joint replacement devices, shoulder joint replacement devices, and pins, braces and plates used to set fractured bones. Some contemporary orthopedic and dental implants, use high performance metals such as cobalt-chrome and titanium alloy to achieve high strength. These materials

are readily fabricated into the complex shapes typical of these devices using mature metal working techniques including casting and machining.

The material surface is coated with an amount of agent effective to repel or attract cells (e.g., immune cells), depending upon the desired therapeutic effect. In important embodiments, the material surface is part of an implant. In important embodiments, in addition to a fugetactic agent, the material surface may also be coated with a cell growth potentiating agent, an anti-infective agent, and/or an anti-inflammatory agent.

A cell-growth potentiating agent as used herein is an agent which stimulates growth of a cell and includes growth factors such as PDGF, EGF, FGF, TGF, NGF, CNTF, and GDNF.

An anti-infectious agent as used herein is an agent which reduces the activity of or kills a microorganism and includes: Aztreonam; Chlorhexidine Gluconate; Imidurea; Lycetamine; Nibroxane; Pirazmonam Sodium; Propionic Acid; Pyrithione Sodium; Sanguinarium Chloride; Tigemonam Dicholine; Acedapsone; Acetosulfone Sodium; Alamecin; Alexidine; Amdinocillin; Amdinocillin Pivoxil; Amicycline; Amifloxacin; Amifloxacin Mesylate; Amikacin; Amikacin Sulfate; Aminosalicylic acid; Aminosalicylate sodium; Amoxicillin; Amphomycin; Ampicillin; Ampicillin Sodium; Apalcillin Sodium; Apramycin; Aspartocin; Astromicin Sulfate; Avilamycin; Avoparcin; Azithromycin; Azlocillin; Azlocillin Sodium; Bacampicillin Hydrochloride; Bacitracin; Bacitracin Methylene Disalicylate; Bacitracin Zinc; Bambermycins; Benzoylpas Calcium; Berythromycin; Betamicin Sulfate; Biapenem; Biniramycin; Biphenamine Hydrochloride; Bispyrithione Magsulfex; Butikacin; Butirosin Sulfate; Capreomycin Sulfate; Carbadox; Carbenicillin Disodium; Carbenicillin Indanyl Sodium; Carbenicillin Phenyl Sodium; Carbenicillin Potassium; Carumonam Sodium; Cefaclor; Cefadroxil; Cefamandole; Cefamandole Nafate; Cefamandole Sodium; Cefaparole; Cefatrizine; Cefazaflur Sodium; Cefazolin; Cefazolin Sodium; Cefbuperazone; Cefdinir; Cefepime; Cefepime Hydrochloride; Cefetecol; Cefixime; Cefmenoxime Hydrochloride; Cefmetazole; Cefmetazole Sodium; Cefonicid Monosodium; Cefonicid Sodium; Cefoperazone Sodium; Ceforanide; Cefotaxime Sodium; Cefotetan; Cefotetan Disodium; Cefotiam Hydrochloride; Cefoxitin; Cefoxitin Sodium; Cefpimizole; Cefpimizole Sodium; Cefpiramide; Cefpiramide Sodium;

Cefpirome Sulfate; Cefpodoxime Proxetil; Cefprozil; Cefroxadine; Cefsulodin Sodium; Ceftazidime; Ceftibuten; Ceftizoxime Sodium; Ceftriaxone Sodium; Cefuroxime; Cefuroxime Axetil; Cefuroxime Pivoxetil; Cefuroxime Sodium; Cephacetrile Sodium; Cephalexin; Cephalexin Hydrochloride; Cephaloglycin; Cephaloridine; Cephalothin Sodium; Cephapirin Sodium; Cephradine; Cetocycline Hydrochloride; Cetophenicol; Chloramphenicol; Chloramphenicol Palmitate; Chloramphenicol Pantothenate Complex; Chloramphenicol Sodium Succinate; Chlorhexidine Phosphanilate; Chloroxylenol; Chlortetracycline Bisulfate; Chlortetracycline Hydrochloride; Cinoxacin; Ciprofloxacin; Ciprofloxacin Hydrochloride; Cirolemycin; Clarithromycin; Clinafloxacin Hydrochloride; Clindamycin; Clindamycin Hydrochloride; Clindamycin Palmitate Hydrochloride; Clindamycin Phosphate; Clofazimine; Cloxacillin Benzathine; Cloxacillin Sodium; Cloxyquin; Colistimethate Sodium; Colistin Sulfate; Coumermycin; Coumermycin Sodium; Cyclacillin; Cycloserine; Dalfopristin; Dapsone; Daptomycin; Demeclocycline; Demeclocycline Hydrochloride; Demecycline; Denofungin; Diaveridine; Dicloxacillin; Dicloxacillin Sodium; Dihydrostreptomycin Sulfate; Dipyrithione; Dirithromycin; Doxycycline; Doxycycline Calcium; Doxycycline Fosfatex; Doxycycline Hyclate; Droxacin Sodium; Enoxacin; Epicillin; Epitetracycline Hydrochloride; Erythromycin; Erythromycin Acistrate; Erythromycin Estolate; Erythromycin Ethylsuccinate; Erythromycin Gluceptate; Erythromycin Lactobionate; Erythromycin Propionate; Erythromycin Stearate; Ethambutol Hydrochloride; Ethionamide; Fleroxacin; Floxacillin; Fludalanine; Flumequine; Fosfomycin; Fosfomycin Tromethamine; Fumoxicillin; Furazolium Chloride; Furazolium Tartrate; Fusidate Sodium; Fusidic Acid; Gentamicin Sulfate; Gloximonam; Gramicidin; Haloprogin; Hetacillin; Hetacillin Potassium; Hexedine; Ibafloxacin; Imipenem; Isoconazole; Isepamicin; Isoniazid; Josamycin; Kanamycin Sulfate; Kitasamycin; Levofuraltadone; Levopropylcillin Potassium; Lexithromycin; Lincomycin; Lincomycin Hydrochloride; Lomefloxacin; Lomefloxacin Hydrochloride; Lomefloxacin Mesylate; Loracarbef; Mafenide; Meclocycline; Meclocycline Sulfosalicylate; Megalomicin Potassium Phosphate; Mequidox; Meropenem; Methacycline; Methacycline Hydrochloride; Methenamine; Methenamine Hippurate; Methenamine Mandelate; Methicillin Sodium; Metioprim; Metronidazole Hydrochloride; Metronidazole Phosphate; Mezlocillin; Mezlocillin

Sodium; Minocycline; Minocycline Hydrochloride; Mirincamycin Hydrochloride; Monensin; Monensin Sodium; Nafcillin Sodium; Nalidixate Sodium; Nalidixic Acid; Natamycin; Nebramycin; Neomycin Palmitate; Neomycin Sulfate; Neomycin Undecylenate; Netilmicin Sulfate; Neutramycin; Nifuradene; Nifuraldezone; Nifuratel; Nifuratrone; Nifurdazil; Nifurimide; Nifurpirinol; Nifurquinazol; Nifurthiazole; Nitrocycline; Nitrofurantoin; Nitromide; Norfloxacin; Novobiocin Sodium; Ofloxacin; Ormetoprim; Oxacillin Sodium; Oximonam; Oximonam Sodium; Oxolinic Acid; Oxytetracycline; Oxytetracycline Calcium; Oxytetracycline Hydrochloride; Paldimycin; Parachlorophenol; Paulomycin; Pefloxacin; Pefloxacin Mesylate; Penamecillin; Penicillin G Benzathine; Penicillin G Potassium; Penicillin G Procaine; Penicillin G Sodium; Penicillin V; Penicillin V Benzathine; Penicillin V Hydrabamine; Penicillin V Potassium; Pentizidone Sodium; Phenyl Aminosalicylate; Piperacillin Sodium; Pirbenicillin Sodium; Piridicillin Sodium; Pirlimycin Hydrochloride; Pivampicillin Hydrochloride; Pivampicillin Pamoate; Pivampicillin Probenate; Polymyxin B Sulfate; Porfiromycin; Propikacin; Pyrazinamide; Pyrithione Zinc; Quindecamine Acetate; Quinupristin; Racephenicol; Ramoplanin; Ranimycin; Relomycin; Repromicin; Rifabutin; Rifametane; Rifamexil; Rifamide; Rifampin; Rifapentine; Rifaximin; Rolitetracycline; Rolitetracycline Nitrate; Rosaramicin; Rosaramicin Butyrate; Rosaramicin Propionate; Rosaramicin Sodium Phosphate; Rosaramicin Stearate; Rosoxacin; Roxarsone; Roxithromycin; Sancycline; Sanfetrinem Sodium; Sarmoxicillin; Sarpicillin; Scopafungin; Sisomicin; Sisomicin Sulfate; Sparfloxacin; Spectinomycin Hydrochloride; Spiramycin; Stallimycin Hydrochloride; Steffimycin; Streptomycin Sulfate; Streptonicozid; Sulfabenz; Sulfabenzamide; Sulfacetamide; Sulfacetamide Sodium; Sulfacytine; Sulfadiazine; Sulfadiazine Sodium; Sulfadoxine; Sulfalene; Sulfamerazine; Sulfameter; Sulfamethazine; Sulfamethizole; Sulfamethoxazole; Sulfamonomethoxine; Sulfamoxole; Sulfanilate Zinc; Sulfanitran; Sulfasalazine; Sulfasomizole; Sulfathiazole; Sulfazamet; Sulfisoxazole; Sulfisoxazole Acetyl; Sulfisoxazole Diolamine; Sulfomyxin; Sulopenem; Sultamicillin; Suncillin Sodium; Talampicillin Hydrochloride; Teicoplanin; Temafloxacin Hydrochloride; Temocillin; Tetracycline; Tetracycline Hydrochloride; Tetracycline Phosphate Complex; Tetroxoprim; Thiamphenicol; Thiphencillin Potassium; Ticarcillin Cresyl Sodium; Ticarcillin Disodium; Ticarcillin

Monosodium; Ticlatone; Tiodonium Chloride; Tobramycin; Tobramycin Sulfate; Tosufloxacin; Trimethoprim; Trimethoprim Sulfate; Trisulfapyrimidines; Troleandomycin; Trospectomycin Sulfate; Tyrothricin; Vancomycin; Vancomycin Hydrochloride; Virginiamycin; Zorbamycin; Difloxacin Hydrochloride; Lauryl Isoquinolinium Bromide; Moxalactam Disodium; Ornidazole; Pentisomicin; and Sarafloxacin Hydrochloride.

An anti-inflammatory agent is an agent that reduces or inhibits altogether an inflammatory response in vivo and includes Alclofenac; Alclometasone Dipropionate; Algestone Acetonide; Alpha Amylase; Amcinafal; Amcinafide; Amfenac Sodium; Amiprilose Hydrochloride; Anakinra; Anirolac; Anitrazafen; Apazone; Balsalazide Disodium; Bendazac; Benoxaprofen; Benzydamine Hydrochloride; Bromelains; Broperamole; Budesonide; Carprofen; Cicloprofen; Cintazone; Cliprofen; Clobetasol Propionate; Clobetasone Butyrate; Clopirac; Cloticasone Propionate; Cormethasone Acetate; Cortodoxone; Deflazacort; Desonide; Desoximetasone; Dexamethasone Dipropionate; Diclofenac Potassium; Diclofenac Sodium; Diflorasone Diacetate; Diflumidone Sodium; Diflunisal; Difluprednate; Diftalone; Dimethyl Sulfoxide; Drocinonide; Endrysone; Enlimomab; Enolicam Sodium; Epirizole; Etodolac; Etofenamate; Felbinac; Fenamole; Fenbufen; Fenclofenac; Fenclorac; Fendosal; Fenpipalone; Fentiazac; Flazalone; Fluazacort; Flufenamic Acid; Flumizole; Flunisolide Acetate; Flunixin; Flunixin Meglumine; Fluocortin Butyl; Fluorometholone Acetate; Fluquazone; Flurbiprofen; Fluretofen; Fluticasone Propionate; Furaprofen; Furobufen; Halcinonide; Halobetasol Propionate; Halopredone Acetate; Ibufenac; Ibuprofen; Ibuprofen Aluminum; Ibuprofen Piconol; Ilonidap; Indomethacin; Indomethacin Sodium; Indoprofen; Indoxole; Intrazole; Isoflupredone Acetate; Isoxepac; Isoxicam; Ketoprofen; Lofemizole Hydrochloride; Lornoxicam; Loteprednol Etabonate; Meclofenamate Sodium; Meclofenamic Acid; Meclorisone Dibutyrate; Mefenamic Acid; Mesalamine; Meseclazone; Methylprednisolone Suleptanate; Morniflumate; Nabumetone; Naproxen; Naproxen Sodium; Naproxol; Nimazone; Olsalazine Sodium; Orgotein; Orpanoxin; Oxaprozin; Oxyphenbutazone; Paranyline Hydrochloride; Pentosan Polysulfate Sodium; Phenbutazone Sodium Glycerate; Pirfenidone; Piroxicam; Piroxicam Cinnamate; Piroxicam Olamine; Pirprofen; Prednazate; Prifelone; Prodolic Acid; Proquazone; Proxazole; Proxazole Citrate;

Rimexolone; Romazarit; Salcolex; Salnacedin; Salsalate; Sanguinarium Chloride; Seclazone; Sermetacin; Sudoxicam; Sulindac; Suprofen; Talmetacin; Talniflumate; Talosalate; Tebufelone; Tenidap; Tenidap Sodium; Tenoxicam; Tesicam; Tesimide; Tetrydamine; Tiopinac; Tixocortol Pivalate; Tolmetin; Tolmetin Sodium; Triclonide; Triflumidate; Zidometacin; Zomepirac Sodium.

According to one aspect of the invention, a method of inhibiting migration of immune cells to a specific site in a subject is provided. The method involves locally administering to a specific site in a subject in need of such treatment an agent that promotes fugetaxis in an amount effective to inhibit migration of immune cells to the specific site in a subject.

In one important embodiment, the invention provides a method of inhibiting migration of immune cells to a site of inflammation in the subject. "Inflammation" as used herein, is a localized protective response elicited by a foreign (non-self) antigen, and/or by an injury or destruction of tissue(s), which serves to destroy, dilute or sequester the foreign antigen, the injurious agent, and/or the injured tissue. Inflammation occurs when tissues are injured by viruses, bacteria, trauma, chemicals, heat, cold, or any other harmful stimuli. In such instances, the classic weapons of the immune system (T cells, B cells, macrophages) interface with cells and soluble products that are mediators of inflammatory responses (neutrophils, eosinophils, basophils, kinin and coagulation systems, and complement cascade).

A typical inflammatory response is characterized by (i) migration of leukocytes at the site of antigen (injury) localization; (ii) specific and nonspecific recognition of "foreign" and other (necrotic/injured tissue) antigens mediated by B and T lymphocytes, macrophages and the alternative complement pathway; (iii) amplification of the inflammatory response with the recruitment of specific and nonspecific effector cells by complement components, lymphokines and monokines, kinins, arachidonic acid metabolites, and mast cell/basophil products; and (iv) macrophage, neutrophil and lymphocyte participation in antigen destruction with ultimate removal of antigen particles (injured tissue) by phagocytosis.

According to yet another aspect of the invention, a method of enhancing an immune response in a subject having a condition that involves a specific site, is provided. The method involves locally administering to a specific site in a subject in need of such treatment an agent that inhibits fugetaxis or stimulates chemotaxis in an

amount effective to inhibit immune cell-specific fugetactic activity at a specific site in the subject. In some embodiments, the specific site is a site of a pathogenic infection. Efficient recruitment of immune cells to help eliminate the infection is therefore beneficial.

In certain embodiments, the specific site is a germ cell containing site. In this case the recruitment of immune cells to these specific sites will help eliminate unwanted germ cells, and/or implanted and nonimplanted embryos. In further embodiments, co-administration of contraceptive agents other than anti-fugetactic agents is also provided.

In further embodiments, the specific site is an area immediately surrounding a tumor. Since most of the known tumors escape immune recognition, it is beneficial to enhance the migration of immune cells to the tumor site. In further embodiments, co-administration of anti-cancer agents other than anti-fugetactic agents is also provided. Non-anti-fugetactic anti-cancer agents include: Acivicin; Aclarubicin; Acodazole Hydrochloride; Acronine; Adozelesin; Aldesleukin; Altretamine; Ambomycin; Ametantrone Acetate; Aminoglutethimide; Amsacrine; Anastrozole; Anthramycin; Asparaginase; Asperlin; Azacitidine; Azetepa; Azotomycin; Batimastat; Benzodepa; Bicalutamide; Bisantrene Hydrochloride; Bisnafide Dimesylate; Bizelesin; Bleomycin Sulfate; Brequinar Sodium; Bropirimine; Busulfan; Cactinomycin; Calusterone; Caracemide; Carbetimer; Carboplatin; Carmustine; Carubicin Hydrochloride; Carzelesin; Cedefingol; Chlorambucil; Cirolemycin; Cisplatin; Cladribine; Crisnatol Mesylate; Cyclophosphamide; Cytarabine; Dacarbazine; Dactinomycin; Daunorubicin Hydrochloride; Decitabine; Dexormaplatin; Dezaguanine; Dezaguanine Mesylate; Diaziquone; Docetaxel; Doxorubicin; Doxorubicin Hydrochloride; Droloxifene; Droloxifene Citrate; Dromostanolone Propionate; Duazomycin; Edatrexate; Eflornithine Hydrochloride; Elsamitrucin; Enloplatin; Enpromate; Epipropidine; Epirubicin Hydrochloride; Erbulozole; Esorubicin Hydrochloride; Estramustine; Estramustine Phosphate Sodium; Etanidazole; Etoposide; Etoposide Phosphate; Etoprine; Fadrozole Hydrochloride; Fazarabine; Fenretinide; Floxuridine; Fludarabine Phosphate; Fluorouracil; Flurocitabine; Fosquidone; Fostriecin Sodium; Gemcitabine; Gemcitabine Hydrochloride; Hydroxyurea; Idarubicin Hydrochloride; Ifosfamide; Ilmofosine; Interferon Alfa-2a; Interferon Alfa-2b; Interferon Alfa-n1;

Interferon Alfa-n3; Interferon Beta-I a; Interferon Gamma-I b; Iproplatin; Irinotecan Hydrochloride; Lanreotide Acetate; Letrozole; Leuprolide Acetate; Liarozole Hydrochloride; Lometrexol Sodium; Lomustine; Losoxantrone Hydrochloride; Masoprocol; Maytansine; Mechlorethamine Hydrochloride; Megestrol Acetate; Melengestrol Acetate; Melphalan; Menogaril; Mercaptopurine; Methotrexate; Methotrexate Sodium; Metoprine; Meturedepa; Mitindomide; Mitocarcin; Mitocromin; Mitogillin; Mitomalcin; Mitomycin; Mitosper; Mitotane; Mitoxantrone Hydrochloride; Mycophenolic Acid; Nocodazole; Nogalamycin; Ormaplatin; Oxisuran; Paclitaxel; Pegaspargase; Peliomycin; Pentamustine; Peplomycin Sulfate; Perfosfamide; Pipobroman; Piposulfan; Piroxantrone Hydrochloride; Plicamycin; Plomestane; Podofilox; Porfimer Sodium; Porfiromycin; Prednimustine; Procarbazine Hydrochloride; Puromycin; Puromycin Hydrochloride; Pyrazofurin; Riboprine; Rogletimide; Safingol; Safingol Hydrochloride; Semustine; Simtrazene; Sparfosate Sodium; Sparsomycin; Spirogermanium Hydrochloride; Spiromustine; Spiroplatin; Streptonigrin; Streptozocin; Sulofenur; Talisomycin; Taxotere; Tecogalan Sodium; Tegafur; Teloxantrone Hydrochloride; Temoporfin; Teniposide; Teroxirone; Testolactone; Thiamiprine; Thioguanine; Thiotepa; Tiazofurin; Tirapazamine; Topotecan Hydrochloride; Toremifene Citrate; Trestolone Acetate; Triciribine Phosphate; Trimetrexate; Trimetrexate Glucuronate; Triptorelin; Tubulozole Hydrochloride; Uracil Mustard; Uredepa; Vapreotide; Verteporfin; Vinblastine Sulfate; Vincristine Sulfate; Vindesine; Vindesine Sulfate; Vinepidine Sulfate; Vinglycinate Sulfate; Vinleurosine Sulfate; Vinorelbine Tartrate; and Vinrosidine Sulfate.

In some embodiments, the fugetaxis stimulating, fugetaxis inhibiting, chemotaxis stimulating or chemotaxis inhibiting agents of the invention are administered substantially simultaneously with other therapeutic agents. By "substantially simultaneously," it is meant that the agents are administered to the subject close enough in time, so that the other therapeutic agents may exert a potentiating effect on migration inhibiting or stimulating activity of the fugetactic or chemotactic agent. The fugetactic or chemotactic agent may be administered before, at the same time, and/or after the administration of the other therapeutic agent.

The methods provided herein in some instances may be carried out by administration of antisense molecules in order to block transcription or translation of

nucleic acid expression products. As used herein, the term "antisense oligonucleotide" or "antisense" describes an oligonucleotide that is an oligoribonucleotide, oligodeoxyribonucleotide, modified oligoribonucleotide, or modified oligodeoxyribonucleotide which hybridizes under physiological conditions to DNA comprising a particular gene or to an mRNA transcript of that gene and, thereby, inhibits the transcription of that gene and/or the translation of that mRNA. The antisense molecules are designed so as to interfere with transcription or translation of a target gene upon hybridization with the target gene or transcript. Those skilled in the art will recognize that the exact length of the antisense oligonucleotide and its degree of complementarity with its target will depend upon the specific target selected, including the sequence of the target and the particular bases which comprise that sequence.

It is preferred that the antisense oligonucleotide be constructed and arranged so as to bind selectively with the target under physiological conditions, i.e., to hybridize substantially more to the target sequence than to any other sequence in the target cell under physiological conditions. Based upon the identification of molecules that are upregulated in fugetaxis or chemotaxis (see the Tables herein), one of skill in the art can easily choose and synthesize any of a number of appropriate antisense molecules for use in accordance with the present invention. In order to be sufficiently selective and potent for inhibition, such antisense oligonucleotides should comprise at least about 10 and, more preferably, at least about 15 consecutive bases which are complementary to the target, although in certain cases modified oligonucleotides as short as 7 bases in length have been used successfully as antisense oligonucleotides. See Wagner et al., Nat. Med. 1(11):1116-1118, 1995. Most preferably, the antisense oligonucleotides comprise a complementary sequence of 20-30 bases. Although oligonucleotides may be chosen which are antisense to any region of the gene or mRNA transcripts, in preferred embodiments the antisense oligonucleotides correspond to N-terminal or 5' upstream sites such as translation initiation, transcription initiation or promoter sites. In addition, 3'-untranslated regions may be targeted by antisense oligonucleotides. Targeting to mRNA splicing sites has also been used in the art but may be less preferred if alternative mRNA splicing occurs. In addition, the antisense is targeted, preferably, to sites in which mRNA secondary structure is not expected (see, e.g.,

Sainio et al., Cell Mol. Neurobiol. 14(5):439-457, 1994) and at which proteins are not expected to bind.

In one set of embodiments, the antisense oligonucleotides of the invention may be composed of "natural" deoxyribonucleotides, ribonucleotides, or any combination thereof. That is, the 5' end of one native nucleotide and the 3' end of another native nucleotide may be covalently linked, as in natural systems, via a phosphodiester internucleoside linkage. These oligonucleotides may be prepared by art recognized methods which may be carried out manually or by an automated synthesizer. They also may be produced recombinantly by vectors.

In preferred embodiments, however, the antisense oligonucleotides of the invention also may include "modified" oligonucleotides. That is, the oligonucleotides may be modified in a number of ways which do not prevent them from hybridizing to their target but which enhance their stability or targeting or which otherwise enhance their therapeutic effectiveness..

The term "modified oligonucleotide" as used herein describes an oligonucleotide in which (1) at least two of its nucleotides are covalently linked via a synthetic internucleoside linkage (i.e., a linkage other than a phosphodiester linkage between the 5' end of one nucleotide and the 3' end of another nucleotide) and/or (2) a chemical group not normally associated with nucleic acid molecules has been covalently attached to the oligonucleotide. Preferred synthetic internucleoside linkages are phosphorothioates, alkylphosphonates, phosphorodithioates, phosphate esters, alkylphosphonothioates, phosphoramidates, carbamates, carbonates, phosphate triesters, acetamidates, carboxymethyl esters and peptides.

The term "modified oligonucleotide" also encompasses oligonucleotides with a covalently modified base and/or sugar. For example, modified oligonucleotides include oligonucleotides having backbone sugars which are covalently attached to low molecular weight organic groups other than a hydroxyl group at the 3' position and other than a phosphate group at the 5' position. Thus modified oligonucleotides may include a 2'-O-alkylated ribose group. In addition, modified oligonucleotides may include sugars such as arabinose instead of ribose.

The present invention, thus, contemplates pharmaceutical preparations containing modified antisense molecules together with pharmaceutically acceptable carriers. Antisense oligonucleotides may be administered as part of a

pharmaceutical composition. In this latter embodiment, it is preferable that a slow intravenous administration be used. Such a pharmaceutical composition may include the antisense oligonucleotides in combination with any standard physiologically and/or pharmaceutically acceptable carriers which are known in the art. The compositions should be sterile and contain a therapeutically effective amount of the antisense oligonucleotides in a unit of weight or volume suitable for administration to a patient.

The compositions, as described above, are administered in effective amounts. The effective amount will depend upon the mode of administration, the particular condition being treated and the desired outcome. It will also depend upon, as discussed above, the stage of the condition, the age and physical condition of the subject, the nature of concurrent therapy, if any, and like factors well known to the medical practitioner. For therapeutic applications, it is that amount sufficient to achieve a medically desirable result. In some cases this is a local (site-specific) reduction of inflammation. In other cases, it is inhibition of tumor growth and/or metastasis. In still other embodiments, the effective amount is that amount sufficient for stimulating an immune response leading to the inhibition of an infection, or a cancer.

Generally, doses of active compounds of the present invention would be from about 0.01 mg/kg per day to 1000 mg/kg per day. It is expected that doses ranging from 50-500 mg/kg will be suitable. A variety of administration routes are available. The methods of the invention, generally speaking, may be practiced using any mode of administration that is medically acceptable, meaning any mode that produces effective levels of the active compounds without causing clinically unacceptable adverse effects. Such modes of administration include oral, rectal, topical, nasal, interdermal, or parenteral routes. The term "parenteral" includes subcutaneous, intravenous, intramuscular, or infusion. Intravenous or intramuscular routes are not particularly suitable for long-term therapy and prophylaxis. They could, however, be preferred in emergency situations. Oral administration will be preferred for prophylactic treatment because of the convenience to the patient as well as the dosing schedule. When peptides are used therapeutically, in certain embodiments a desirable route of administration is by pulmonary aerosol. Techniques for preparing aerosol delivery systems containing peptides are well

known to those of skill in the art. Generally, such systems should utilize components which will not significantly impair the biological properties of the antibodies, such as the paratope binding capacity (see, for example, Sciarra and Cutie, "Aerosols," in Remington's Pharmaceutical Sciences, 18th edition, 1990, pp 1694-1712; incorporated by reference). Those of skill in the art can readily determine the various parameters and conditions for producing antibody or peptide aerosols without resort to undue experimentation.

Compositions suitable for oral administration may be presented as discrete units, such as capsules, tablets, lozenges, each containing a predetermined amount of the active agent. Other compositions include suspensions in aqueous liquids or non-aqueous liquids such as a syrup, elixir or an emulsion.

Preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's or fixed oils. Intravenous vehicles include fluid and nutrient replenishers, electrolyte replenishers (such as those based on Ringer's dextrose), and the like. Preservatives and other additives may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, and inert gases and the like. Lower doses will result from other forms of administration, such as intravenous administration. In the event that a response in a subject is insufficient at the initial doses applied, higher doses (or effectively higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits. Multiple doses per day are contemplated to achieve appropriate systemic levels of compounds.

The agents may be combined, optionally, with a pharmaceutically-acceptable carrier. The term "pharmaceutically-acceptable carrier" as used herein means one or more compatible solid or liquid filler, diluents or encapsulating substances which are suitable for administration into a human. The term "carrier" denotes an organic or inorganic ingredient, natural or synthetic, with which the active ingredient is combined to facilitate the application. The components of the pharmaceutical

compositions also are capable of being co-mingled with the molecules of the present invention, and with each other, in a manner such that there is no interaction which would substantially impair the desired pharmaceutical efficacy.

The invention in other aspects includes pharmaceutical compositions of the agents.When administered, the pharmaceutical preparations of the invention are applied in pharmaceutically-acceptable amounts and in pharmaceutically-acceptably compositions. Such preparations may routinely contain salt, buffering agents, preservatives, compatible carriers, and optionally other therapeutic agents. When used in medicine, the salts should be pharmaceutically acceptable, but non-pharmaceutically acceptable salts may conveniently be used to prepare pharmaceutically-acceptable salts thereof and are not excluded from the scope of the invention. Such pharmacologically and pharmaceutically-acceptable salts include, but are not limited to, those prepared from the following acids: hydrochloric, hydrobromic, sulfuric, nitric, phosphoric, maleic, acetic, salicylic, citric, formic, malonic, succinic, and the like. Also, pharmaceutically-acceptable salts can be prepared as alkaline metal or alkaline earth salts, such as sodium, potassium or calcium salts.

Various techniques may be employed for introducing nucleic acids of the invention (e.g., antisense nucleic acids) into cells, depending on whether the nucleic acids are introduced in vitro or in vivo in a host. Such techniques include transfection of nucleic acid-$CaPO_4$ precipitates, transfection of nucleic acids associated with DEAE, transfection with a retrovirus including the nucleic acid of interest, liposome mediated transfection, and the like. For certain uses, it is preferred to target the nucleic acid to particular cells. In such instances, a vehicle used for delivering a nucleic acid of the invention into a cell (e.g., a retrovirus, or other virus; a liposome) can have a targeting molecule attached thereto. For example, a molecule such as an antibody specific for a surface membrane protein on the target cell or a ligand for a receptor on the target cell can be bound to or incorporated within the nucleic acid delivery vehicle. For example, where liposomes are employed to deliver the nucleic acids of the invention, proteins which bind to a surface membrane protein associated with endocytosis may be incorporated into the liposome formulation for targeting and/or to facilitate uptake. Such proteins include capsid proteins or fragments thereof tropic for a particular cell type,

antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half life, and the like. Polymeric delivery systems also have been used successfully to deliver nucleic acids into cells, as is known by those skilled in the art. Such systems even permit oral delivery of nucleic acids.

Other delivery systems can include time-release, delayed release or sustained release delivery systems (collectively referred to herein as controlled release). Such systems can avoid repeated administrations of the fugetactic agent, increasing convenience to the subject and the physician. Many types of release delivery systems are available and known to those of ordinary skill in the art. They include polymer base systems such as poly(lactide-glycolide), copolyoxalates, polycaprolactones, polyesteramides, polyorthoesters, polyhydroxybutyric acid, and polyanhydrides. Microcapsules of the foregoing polymers containing drugs are described in, for example, U.S. Patent 5,075,109. Delivery systems also include non-polymer systems that are: lipids including sterols such as cholesterol, cholesterol esters and fatty acids or neutral fats such as mono- di- and tri-glycerides; hydrogel release systems; sylastic systems; peptide based systems; wax coatings; compressed tablets using conventional binders and excipients; partially fused implants; and the like. Specific examples include, but are not limited to: (a) erosional systems in which the anti-inflammatory agent is contained in a form within a matrix such as those described in U.S. Patent Nos. 4,452,775, 4,667,014, 4,748,034 and 5,239,660 and (b) difusional systems in which an active component permeates at a controlled rate from a polymer such as described in U.S. Patent Nos. 3,832,253, and 3,854,480.

A preferred delivery system of the invention is a colloidal dispersion system. Colloidal dispersion systems include lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system of the invention is a liposome. Liposomes are artificial membrane vessels which are useful as a delivery vector in vivo or in vitro. It has been shown that large unilamellar vessels (LUV), which range in size from 0.2 - 4.0 μm can encapsulate large macromolecules. RNA, DNA, and intact virions can be encapsulated within the aqueous interior and be delivered to cells in a biologically active form (Fraley, et al., Trends Biochem. Sci., (1981) 6:77). In order for a liposome to be an efficient

gene transfer vector, one or more of the following characteristics should be present: (1) encapsulation of the gene of interest at high efficiency with retention of biological activity; (2) preferential and substantial binding to a target cell in comparison to non-target cells; (3) delivery of the aqueous contents of the vesicle to the target cell cytoplasm at high efficiency; and (4) accurate and effective expression of genetic information.

Liposomes may be targeted to a particular tissue by coupling the liposome to a specific ligand such as a monoclonal antibody, sugar, glycolipid, or protein. Liposomes are commercially available from Gibco BRL, for example, as LIPOFECTIN™ and LIPOFECTACE™, which are formed of cationic lipids such as N-[1-(2, 3 dioleyloxy)-propyl]-N, N, N-trimethylammonium chloride (DOTMA) and dimethyl dioctadecylammonium bromide (DDAB). Methods for making liposomes are well known in the art and have been described in many publications. Liposomes also have been reviewed by Gregoriadis, G. in Trends in Biotechnology, (1985) 3:235-241.

In one important embodiment, the preferred vehicle is a biocompatible microparticle or implant that is suitable for implantation into the mammalian recipient. Exemplary bioerodible implants that are useful in accordance with this method are described in PCT International application no. PCT/US/03307 (Publication No. WO 95/24929, entitled "Polymeric Gene Delivery System"). PCT/US/0307 describes a biocompatible, preferably biodegradable polymeric matrix for containing an exogenous gene under the control of an appropriate promoter. The polymeric matrix is used to achieve sustained release of the exogenous gene in the patient. In accordance with the instant invention, the fugetactic agents described herein are encapsulated or dispersed within the biocompatible, preferably biodegradable polymeric matrix disclosed in PCT/US/03307.

The polymeric matrix preferably is in the form of a microparticle such as a microsphere (wherein an agent is dispersed throughout a solid polymeric matrix) or a microcapsule (wherein an agent is stored in the core of a polymeric shell). Other forms of the polymeric matrix for containing an agent include films, coatings, gels, implants, and stents. The size and composition of the polymeric matrix device is selected to result in favorable release kinetics in the tissue into which the matrix is introduced. The size of the polymeric matrix further is selected according to the

method of delivery which is to be used. Preferably when an aerosol route is used the polymeric matrix and fugetactic agent are encompassed in a surfactant vehicle. The polymeric matrix composition can be selected to have both favorable degradation rates and also to be formed of a material which is bioadhesive, to further increase the effectiveness of transfer. The matrix composition also can be selected not to degrade, but rather, to release by diffusion over an extended period of time.

In another important embodiment the delivery system is a biocompatible microsphere that is suitable for local, site-specific delivery. Such microspheres are disclosed in Chickering et al., Biotech. And Bioeng., (1996) 52:96-101 and Mathiowitz et al., Nature, (1997) 386:.410-414.

Both non-biodegradable and biodegradable polymeric matrices can be used to deliver the agents of the invention to the subject. Biodegradable matrices are preferred. Such polymers may be natural or synthetic polymers. Synthetic polymers are preferred. The polymer is selected based on the period of time over which release is desired, generally in the order of a few hours to a year or longer. Typically, release over a period ranging from between a few hours and three to twelve months is most desirable. The polymer optionally is in the form of a hydrogel that can absorb up to about 90% of its weight in water and further, optionally is cross-linked with multi-valent ions or other polymers.

In general, fugetactic agents are delivered using a bioerodible implant by way of diffusion, or more preferably, by degradation of the polymeric matrix. Exemplary synthetic polymers which can be used to form the biodegradable delivery system include: polyamides, polycarbonates, polyalkylenes, polyalkylene glycols, polyalkylene oxides, polyalkylene terepthalates, polyvinyl alcohols, polyvinyl ethers, polyvinyl esters, poly-vinyl halides, polyvinylpyrrolidone, polyglycolides, polysiloxanes, polyurethanes and co-polymers thereof, alkyl cellulose, hydroxyalkyl celluloses, cellulose ethers, cellulose esters, nitro celluloses, polymers of acrylic and methacrylic esters, methyl cellulose, ethyl cellulose, hydroxypropyl cellulose, hydroxy-propyl methyl cellulose, hydroxybutyl methyl cellulose, cellulose acetate, cellulose propionate, cellulose acetate butyrate, cellulose acetate phthalate, carboxylethyl cellulose, cellulose triacetate, cellulose sulphate sodium salt, poly(methyl methacrylate), poly(ethyl methacrylate), poly(butylmethacrylate), poly(isobutyl methacrylate), poly(hexylmethacrylate), poly(isodecyl methacrylate),

poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecyl acrylate), polyethylene, polypropylene, poly(ethylene glycol), poly(ethylene oxide), poly(ethylene terephthalate), poly(vinyl alcohols), polyvinyl acetate, poly vinyl chloride, polystyrene, polyvinylpyrrolidone, and polymers of lactic acid and glycolic acid, polyanhydrides, poly(ortho)esters, poly(butic acid), poly(valeric acid), and poly(lactide-cocaprolactone), and natural polymers such as alginate and other polysaccharides including dextran and cellulose, collagen, chemical derivatives thereof (substitutions, additions of chemical groups, for example, alkyl, alkylene, hydroxylations, oxidations, and other modifications routinely made by those skilled in the art), albumin and other hydrophilic proteins, zein and other prolamines and hydrophobic proteins, copolymers and mixtures thereof. In general, these materials degrade either by enzymatic hydrolysis or exposure to water in vivo, by surface or bulk erosion.

Examples of non-biodegradable polymers include ethylene vinyl acetate, poly(meth)acrylic acid, polyamides, copolymers and mixtures thereof.

Bioadhesive polymers of particular interest include bioerodible hydrogels described by H.S. Sawhney, C.P. Pathak and J.A. Hubell in Macromolecules, (1993) 26:581-587, the teachings of which are incorporated herein, polyhyaluronic acids, casein, gelatin, glutin, polyanhydrides, polyacrylic acid, alginate, chitosan, poly(methyl methacrylates), poly(ethyl methacrylates), poly(butylmethacrylate), poly(isobutyl methacrylate), poly(hexylmethacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), and poly(octadecyl acrylate).

In addition, important embodiments of the invention include pump-based hardware delivery systems, some of which are adapted for implantation. Such implantable pumps include controlled-release microchips. A preferred controlled-release microchip is described in Santini, JT Jr., et al., Nature, 1999, 397:335-338, the contents of which are expressly incorporated herein by reference.

Use of a long-term sustained release implant may be particularly suitable for treatment of chronic conditions. Long-term release, are used herein, means that the implant is constructed and arranged to delivery therapeutic levels of the active ingredient for at least 30 days, and preferably 60 days. Long-term sustained release

implants are well-known to those of ordinary skill in the art and include some of the release systems described above.

In certain embodiments, the agents of the invention are delivered directly to the site at which there is inflammation, e.g., the joints in the case of a subject with rheumatoid arthritis, the blood vessels of an atherosclerotic organ, etc. For example, this can be accomplished by attaching an agent (nucleic acid or polypeptide) to the surface of a balloon catheter; inserting the catheter into the subject until the balloon portion is located at the site of inflammation, e.g. an atherosclerotic vessel, and inflating the balloon to contact the balloon surface with the vessel wall at the site of the occlusion. In this manner, the compositions can be targeted locally to particular inflammatory sites to modulate immune cell migration to these sites. In another example the local administration involves an implantable pump to the site in need of such treatment. Preferred pumps are as described above. In a further example, when the treatment of an abscess is involved, the fugetactic agent may be delivered topically, e.g., in an ointment/dermal formulation. Optionally, the agents are delivered in combination with other therapeutic agents (e.g., anti-inflammatory agents, immunosuppressant agents, etc.).

The invention will be more fully understood by reference to the following examples. These examples, however, are merely intended to illustrate the embodiments of the invention and are not to be construed to limit the scope of the invention.

EXAMPLE 1

Example 1 describes experiments and findings that demonstrate that bi-directional migratory response of T cells to specific gradients of the chemokine are associated with differential changes in the expression of genes encoding proteins involved in SDF-1/CXCR4 signal transduction pathway.

Methods

Primary murine or human T cells were exposed to specific gradients of SDF-1 to induce chemotaxis or fugetaxis in vitro and in vivo. The Zigmund/Hirsch chamber and microfabricated devices as well as a murine model of allergic peritonitis were used to establish defined SDF-1 gradients in vitro and in vivo, respectively. Purified T cells were generated from these systems and unamplified RNA examined using genomic array technology (Affymetrix). These results were

validated by RT-PCR and Northern blotting. Control experiments were performed on T cells which had not been exposed to SDF-1 or which had been exposed to the chemokine in the absence of a gradient.

Cell Cultures: CD4+CD45+RA cells were obtained from peripheral blood Buffy coat samples from healthy donors.

Transwell Assays: Transwell assays were done using 0.4 μm pore size filters (23 mm diameter, with polycarbonate membrane; Corning Inc., New York). 10 x 106 cells suspended in 0.5% FBS-containing IMDM were added to the upper chamber of the transwell. To create positive, negative, uniform, and absent gradients, either of 0.5% FBS IMDM medium alone or medium plus SDF-1α.

Total RNA Extraction: Total RNA was extracted from all samples using Gibco's TRIzol protocol (GIBC-BRL, Life Technologies, Rockville, MD) with 1 mL Trizol per 10-20 x 10^6 cells. Total RNA was brought to a concentration of 1 μg/μL and 5-10 μg were used on the Affymetrix chips.

cRNA Preparation and Chip Hybridization Conditions: cRNA probes were prepared according to the GeneChip Expression Analysis Technical Manual and as described previously (Warrington et al. 2000). Briefly, 5-10 μg of total RNA was used to synthesize double-stranded cDNA using SuperScript Choice System (GIBCO-BRL) and a T7-(dT)-24 primer (Geneset Oligos, La Jolla, CA). The cDNA was purified by phenol/chloroform/isoamyl alcohol extraction with Phase Lock Gel (5Prime 3Prime, Boulder, CO) and concentrated by EtOH precipitation. In vitro transcription produced biotin-labeled cRNA using a BioArray HighYield RNA Transcript Labeling Kit (Affymetrix) according to the manufacturer's instructions. cRNA was linearly amplified with T7 polymerase, the biotinylated cRNA was cleaned with RNeasy Mini kit (Qiagen), and 20 μg of labeled cRNA was fragmented (Warrington et al. 2000). The fragmented cRNA was hybridized to the microarray for 16 hours at 45°C with a constant rotation of 60 rpm in the GeneChip Hybridization Oven 640 (Affymetrix). After being washed, the arrays were stained with streptavidin-phycoerythrin (Molecular Probes, Eugene, OR) and amplified by biotinylated anti-streptavidin (Vector Laboratories, Burlingame, CA) using the GeneChip Fluidics Station 400 (Affymetrix), and scanned on the GeneArray scanner (Affymetrix). The intensity for each feature of the array was captured with

Affymetrix GeneChip Software v5.0, according to standard Affymetrix procedures (Warrington et al. 2000).

Statistical Analysis of Expression Data: To enable comparison between experiments, Affymetrix image (.cel) files were loaded into the Rosetta Resolver v4.0 Expression Data Analysis System and normalized according to the Resolver error model (see Waring et al. 2001, Lock et al. 2002 for description).

Q-PCR Verification of Gene Targets: Total RNA from primary T cells was isolated, purified, and quantified as described above. QRT-PCR was performed using the Brilliant One-Setp QRT-PCR kit (Stratagene, La Jolla, CA) containing SYBR Green I (1:30,000, Molecular Probes), forward and reverse primers (50 nM each; Invitrogen), and sample RNA (amount was variable, depending on the transcript abundance).

Results

Chips of the same condition were combined using Rosetta's Resolver error-model based software, as described in the Methods. The combined experiments were then compared between each other in different combinations in order to address distinct sub-components of the hypothesis: M/M - basal conditions; CM - chemokinesis; CT - chemotaxis in positive SDF-1 gradient; and FT - fugetaxis in negative SDF-1 gradient.

The gene expression profile for T cells which underwent chemotaxis differed from the profile generated for T cells which underwent fugetaxis in response to gradients of SDF-1 in several significant respects. Cluster analysis of gene expression demonstrated that genes encoding molecules known to be involved in SDF-1 signal transduction were significantly and differentially expressed ($p \leq 0.05$ for 1.7 to 21 fold changes in RNA expression) when cells which had undergone fugetaxis or chemotaxis were compared. Of particular note, these differentially expressed genes encoded members of the G-protein-coupled receptor kinase, cellular tyrosine kinase, PI-3 kinase and Rho GTPase cascades as well as the cyclic nucleotide metabolic pathway. The gene expression profile for control T cells exposed to SDF-1 in the absence of a gradient also differed from profiles generated from cells responding to gradients of the chemokine.

The data are presented in Tables 1-6 (Figures 3-8).

Signaling molecules that are upregulated in a uniform gradient of SDF-1 (chemokinetic) gradient of SDF-1 include PTK2 (+ 6.88) and Regulator of G-protein signaling 10 (+ 2.53).

Signaling molecules that are downregulated in a uniform gradient of SDF-1 (chemokinetic) gradient of SDF-1 include Phospholipase C, beta 3 (-2.54), RAS p21 protein activator (GAP) 3 (-2.20), Ras guanyl releasing protein 2 (calcium/DAG) (-2.16), G protein-coupled receptor kinase 6 (-2.15), Rho-specific GEF (p114) (-1.70), Protein kinase C substrate 80K-H (-1.70).

Signaling molecules that are upregulated in the presence of a directional (chemotactic and fugetactic) versus neutral (chemokinetic) gradient include Transforming growth factor, beta 1 (1.92 Chemokinetic vs Chemotactic; 1.70 Chemo Fugetactic) and Guanine nucleotide binding protein (1.74 Chemokinetic vs Chemotactic; 1.78 Chemokinetic vs Fugetactic).

Signaling molecules that are downregulated in the presence of a directional (chemotactic and fugetactic) versus neutral (chemokinetic) gradient include Allograft inflammatory factor 1 (-12.9 Chemokinetic vs Chemotactic; -11.9 Chemokinetic vs Fugetactic), Phosphoserine phosphatase-like (- 4.24 Chemokinetic vs Chemotactic; -5.76 Chemokinetic vs Fugetactic) BCR downstream signaling 1 (-1.86 Chemokinetic vs Chemotactic; -2.14 Chemokinetic vs Fugetactic) v-Kit-ras2 Kirsten rat sarcoma 2 viral oncogene (-1.84 Chemokinetic vs Chemotactic; -1.95 Chemokinetic vs Fugetactic).

Signaling molecules differentially expressed between a positive (chemotactic) and a negative (fugetactic) gradient of SDF-1.

Signaling molecules that are more highly expressed in a chemotactic gradient of SDF-1 (versus a fugetactic gradient) include PTK2 (focal adhesion kinase) (8.59), MAP kinase kinase kinase kinase 2 (7.30), Guanine nucleotide binding protein (4.95), PT phosphatase receptor (4.20), CDC42-binding protein kinase beta (3.23), Ral GEF (RalGPS1A) (2.81), MAP kinase 7 (2.78), Autotaxin (2.63), Inositol 1,4,5-triphosphate receptor (2.60), Phosphoinositide-3-kinase, gamma (2.48), PT phosphatase, non-receptor (2.02), Ras p21 protein activator (GAP) (1.98), Ras guanyl releasing protein 2 (1.98) and Arp23 complex 20 kDa subunit (1.95).

Signaling molecules that are more highly expressed in a fugetactic gradient of SDF-1 (versus a chemotactic gradient) include Cell division cycle 42 (4.93),

Ribosomal protein S6 kinase (2.91), BAI1-associated protein 2 (2.84), GTPase regulator associated with FAK (2.59), Protein kinase C, beta 1 (2.16), Phosphoinositide-specific phospholipase C-beta I (1.99), Nitric oxide synthase I (1.99), Phosphatidylinositol-4-phosphate 5-kinase (1.82) and MAP kinase kinase kinase kinase 4 (1.72).

Conclusions

This work elucidates the mechanism of bi-directional T cell migration in vitro and in vivo in response to gradients of SDF-1 and shows that the regulation of gene expression associated with the signal transduction pathway for chemotaxis is distinct from that which is associated with fugetaxis. This work forms the basis for identifying potential molecular targets for specific therapeutic agents which could selectively block or enhance the chemotactic or fugetactic responses of T cells to gradients of SDF-1 in vivo.

EXAMPLE 2

Example 2 describes experiments and findings that demonstrate a new aspect of neutrophil migration in response to the chemokine, Interleukin-8, namely bi-directional movement. Specifically, use of specific non-peptide antagonists of the IL-8 receptor, CXCR2, and known inhibitors of chemokine signal transduction reveal that neutrophils can make a directional decision to move up and down an IL-8 gradient and that this decision is dependent on the steepness of the gradient, the absolute concentration of the chemokine that the neutorphil is exposed to, and the level of occupancy of the CXCR2 receptor. Moreover, the directional decision of neutrophils to migrate down a gradient was also found to be differentially sensitive to signal transduction inhibitors as compared to migration up the gradient.

Methods

Primary human T cells were exposed to specific gradients of IL-8 to induce chemotaxis or fugetaxis *in vitro* and *in vivo* in microfabricated devices. Intravital microscopy and digital image analysis were used to examine neutrophil bi-derectional movement in response to Il-8.

Neutrophil isolation: Human whole blood was obtained from healthy volunteers by venipuncture into tubes containing sodium heparin (Becton Dickinson, San Jose, CA). Whole blood was centrifuged for 4 minutes at 2400 rpm and plasma was removed. Resulting pellet was resuspended in Iscove's Modified Dulbecco's

Medium (IMDM; Cellgro MediaTech, Herndon, VA) with 0.5%(w/v) fetal calf serum (FCS; Cellgro MediaTech). 25 mL of suspension was layered over 10 mL Lymphocyte Separation Medium (ICN, Irvine, CA) and centrifuged for 40 minutes at 1600 rpm at 22°C. Supernatant was aspirated, resulting pellet was resuspended in IMDM with 0.5% (w/v) FCS and 2% (w/v) dextran (Sigma-Aldrich, St. Louis, MO), and red blood cells (RBC) were allowed to sediment for 30 minutes at room temperature. Supernatant was transferred into clean tube and centrifuged for 5 minutes at 2000 rpm. Supernatant was aspirated, pellet was mixed with cold ddH_2O for hypotonic lysis of remaining RBCs, and transferred to IMDM with 0.5% (w/v) FCS. Isolated neutrophils were washed and resuspended in IMDM with 0.5% (w/v) FCS, determined to be 95% pure, and 99% viable by Trypan Blue exclusion.

Fabrication and Preparation of Microfluidic Linear Gradient Generator: The microfluidic linear gradient generator was fabricated in poly(dimethylsiloxane) (PDMS; Sylgard 184, Dow Corning, NY) using rapid prototyping and soft lithography as described previously. Briefly, a high resolution printer was used to generate a transparency mask from a computer-aided design image file. The mask was used in contact photolithography with SU-8 photoresist (Microlithography Chemical Co., Newton MA) to generate a positive relief of patterned photoresist on a silicon wafer. Replicas with embossed channels were fabricated by curing PDMS prepolymer against the patterned wafer. Inlet and outlet ports for media and cell suspension were bored out of the cured PDMS replica using a sharpened syringe needle. The PDMS replica and glass substrate were placed in an oxygen plasma generator (150 mTorr, 100 W) for 1 minute. Immediately following plasma treatment, the PDMS replica and glass were placed against each other and irreversibly bonded. Polyethylene tubing (Becton Dickenson) was inserted into inlet and outlet ports to make the fluidic connections. Tubing was connected to a PHD 2000 syringe pump (Harvard Apparatus, Holliston, MA) to complete the setup. Hemostats were used to control flow during cell loading.

Characterization of Linear Gradient Generator: Verification of gradient formations in the microfluidic device were carried out using solutions of phosphate buffered saline (PBS; Cellgro MediaTech) and fluorescein isothiocynate (FITC; Sigma-Aldrich) as previously described. Verification of gradient formations in the microfluidic device were carried out using solutions of Dulbecco's phosphate buffered saline (DPBS; Cellgro

MediaTech) and fluorescein isothiocynate (FITC; Sigma-Aldrich) as previously described . Briefly, PBS and PBS with 100 μM FITC were introduced into the device. Fluorescent micrographs were taken of the stable gradients at various steady flow speeds (0.1, 1, 10, 100 mm/s). Graphs of the fluorescent intensity profile across the migration channel demonstrate generation of temporally and spatially stable linear gradients; profiles at low flow rates are smooth and continuous, while increased flow speed yields stepped gradients as fluid flow becomes more laminar. (Li Jeon et al, Nat Biotech 2002; Li Jeon et al, Langmuir 2000).

Microfluidic Migration Assay and Timelapse Microscopy : Neutrophils (1 x 10^3 cells) were placed uniformly across the migration channel and allowed to migrate under a linear gradient of human Interleukin-8 (72 a.a.; PeproTech, Rocky Hill, NJ) in IMDM with 0.5% (w/v) FCS flowing at 0.1 mm/sec. Migration was observed in a Nikon Eclipse TE2000-S microscope (Nikon, Japan) through a 10X Plan-Fluor objective (Nikon). Brightfield images were taken every 30 seconds using a C4742-95 Hamamatsu digital camera (Hamamatsu, Japan) controlled by IPLab 3.6.1 (Scanalytics, Fairfax, VA). Cell movement was always observed at a set point along the migration channel. Gradients were also calibrated at this set point. Migration was quantified for all cells across the gradient.

Construction of Digital Videos for Quantitative Analysis: Digital videos were made from time-lapse video microscopy file stacks or S-VHS videotapes using a combination of IPLab 3.6.1, Photoshop 6.0 (Adobe Systems, San Jose, CA), and Apple QuickTime Pro 5.0 (Apple Computer, Cupertino, CA). Migration tracking was carried out using MetaMorph 4.5 (Universal Imaging, Downington, PA.) object tracking application, which generated tables of Cartesian coordinate data for each tracked cell.

Mathematical Analysis of Cell Migration in Linear Gradient Generator: The angular correlation function, or cosine correlation function, was calculated for each experiment. For experiments with no gradient, the correlation function decayed exponentially with increasing time interval, while the function decayed much slower, potentially by a power law, for experiments with a gradient; in all cases correlation of angles over time was increased as absolute [IL-8] increased. The fact that angular choice is correlated over time allowed us to compare angular frequency distributions as an index of directional migration.

Cell movement within the linear gradient generator was characterized based on a biased random walk model (Moghe et al, J Immun Methods 1995; Tan et al, J Biomed Mater Res 2000), thus the movement between tracked positions in

successive frames of a video can be considered as a vector, with a length and associated angle. Tracking data from MetaMorph was analyzed in Excel (Microsoft, USA) and MATLAB 13 (Mathworks, Inc.) to determine mean squared displacements, coefficients of motility, angular frequencies and correlations, random walk path lengths, and migration velocities. Cell motility was characterized as follows. For each cell, the squared displacement $R^2(t)$ was calculated at time interval t,

$$\langle R^2(t)\rangle = \langle (x(t_0 + t) - x(t_0))^2 + (y(t_0 + t) - y(t_0))^2 \rangle,$$

where t_0 is the time at the origin. The origin was shifted along the data set and the displacements were averaged for overlapping time intervals. A global average was performed over all cells in the set to calculate the mean squared displacement. Mathematically modeling cell movement as a correlated, biased random walk, this can be written as

$$\langle R^2(t)\rangle = 2S^2P[t - P(1 - e^{-t/P})],$$

where S and P are measures of the rate of movement and persistence time respectively. When time interval t is much greater than persistence time P, the mean squared displacement becomes linearly proportional to t, analogous to Brownian diffusion,

$$\langle R^2(t)\rangle = 2S^2Pt = 4\mu t$$

where μ is the motility coefficient. The slope and intercept of a least squares regression fitted to the linear section of the mean squared displacement give an estimate of μ and P, respectively. Additionally, a "persistence index" (PI) of the motion or mean free path, was calculated as the total displacement of the cell divided by the total distance traveled along the track. The PI is an indicator of turning behavior, with 1 indicating motion in a straight line and 0 indicating no net displacement.

The directional bias of cell motility was quantified as follows. For each cell, histograms of angle frequency show the distribution of angles associated with each displacement vector between successive time intervals of migration. The binning of these histograms can be varied to reduce the stochastic noise associated with a random walk. The x-axes of these histograms are folded around one point to create

a circular histogram presenting the angular frequencies in 360°. The angular correlation function (or cosine correlation function) was calculated as:

$$g(\tau) = <\varphi(t).\varphi(t+\tau)> = <\cos[\varphi(t) - \varphi(t+\tau)]>,$$

where $\varphi(t)$ is the angle that the displacement vector makes with respect to the direction of the gradient. The decay of this function with increasing time interval indicates the correlation between successive turn angles and is a measure of the directional persistence or memory of the cells. To quantify directional bias with respect to the established gradient, we calculated the "mean chemotropism index" (MCI), which is defined as the net path length traversed by a cell with respect to the direction of the established gradient divided by the total distance traveled and is a measure of the accuracy of orientation.

$$CI = \frac{\sum l_i \cos\varphi_i}{\sum l_i}$$

The index for each cell was calculated and then averaged over the whole population. The average chemotropism index will be 1 if cells are moving directly up the gradient, 0 if there is no preferred orientation, and -1 for migration directly down the gradient.

Signaling Pathway Inhibitors: Cells were treated with pertussis toxin (100 ng/mL; 30 minutes at 37°C), wortmannin (1 μM, 10 μM; 20 minutes at 37°C, 8-Br-cAMP (1 mM; 15 minutes at room temperature), 8-Br-cGMP(1 mM; 15 minutes at room temperature) (Sigma-Aldrich), or the CXCR2 non-peptide antagonist, SB225002 (1pM, 100 pM, 1nM, or 1μM for 15 minutes at 37°C; Calbiochem, CA). Immediately after treatment, cells were seeded in migration channel of the microfluidic device and allowed to migrate as described above.

Intravital Microscopy: Male Sprague Dawley rats (200-300g) were purchased from Harlan-Olac (Bicester, U.K.). Male rats were prepared for intravital microscopy. Briefly, following sedation with i.m. Hypnorm (fentanyl-fluanisone mixture, 0.1 ml; Janssen-Cilag, High Wycombe, U.K.), animals were anesthetized with i.v. sodium pentobarbitone (30 mg/kg loading dose followed by 30 mg/kg/h; Rhône Mérieux, Harlow, U.K). The animals were maintained at 37°C on a custom-built heated microscope stage. Following midline abdominal incision, the mesentery adjoining the terminal ileum was carefully arranged over a glass window in the microscope stage and pinned in position. The mesentery was kept warm and moist by continuous application of Tyrode's balanced salt solution (Sigma Aldrich). Mesenteric post-capillary venules (15-40 μm in diameter) were viewed on an upright fixed-stage microscope (Axioskop FS, Carl Zeiss, Welwyn Garden City, U.K.) fitted with water immersion objectives. Images were captured with a digital camera (C5810-01, Hamamatsu Photonics U.K., Enfield, U.K.) for viewing on a monitor (PVM-1453 MD, Sony U.K., Weybridge, U.K.) and storage by videocassette recorder (AG-MD830E, Panasonic U.K., Bracknell, U.K.). As the resolution of intravital microscopy does not allow definitive distinctions to be made between different subpopulations of leukocytes, all responses are quantified in terms of leukocyte behaviour. Hence, rolling leukocytes were defined as those cells moving slower than the flowing erythrocytes, and rolling flux was quantified as the number of rolling cells moving past a fixed point on the venular wall per minute, averaged for 4-5 min. Firmly adherent leukocytes were defined as those that remained stationary for at least 30 s within a 100-μm segment of a venule. Extravasated leukocytes were defined as those in the perivenular tissue adjacent to, but remaining within a distance of 150 μm of a 100-μm length of vessel segment under study. After baseline readings of rolling, adhesion and transmigration were taken; CINC-1 at final concentrations of 10^{-9} M, 10^{-8} M or 10^{-7} M (Peprotech) was applied topically to the mesenteric tissue in the superfusion buffer. Leukocyte responses within the chosen vessels were quantified for up to 180 minutes, during which the topical application of CINC-1 was maintained. In each animal, multiple vessel segments from appropriate vessels were quantified. Videos of migrating cells were constucted for quantitative and mathematical analysis as described above; at the end of certain in vivo experiments, the mesentery was stained with acridine orange (Sigma Aldrich), a nuclear dye, scanned with a 488 nm laser line generated from an Argon laser,

and observed by confocal microscopy (LSM5 PASCAL, Axioskop II FS, Carl Zeiss) to verify that migrating cells were neutrophils.

Mathematical Modeling of Continuous Gradients in vivo: The chemokine concentration profile in the mesentery at steady state was predicted using a novel in vivo model based on classical diffusion equations applied on a spherical model of the postcapillary venule, and the assumption that the receptor-dependent transport of the chemokine by the endothelial cells is the main mechanism for generating the gradient the vicinity of postcapillary venules. The steady state solution was calculated for the concentration gradient around a sphere in a homogenous medium, with the two boundary conditions: 1) the concentration far from the sphere is constant, and 2) the chemokine flux across the surface of the sphere also constant. Other mechanisms of chemokine transport out of the tissue were considered less significant due to the low lipid solubility of CINC-1 and IL-8 and the presence of tight intercellular junctions between endothelial cells in the absence of vasoactive signals (Middleton et al, Cell 1997). Thus, the steady state concentration C at distance r from the capillary wall was calculated as:

$$C(r) = C_0 - \frac{F_0 a^2}{D(r+a)},$$

where, C_0 is the chemokine concentration in the perfusion solution (either 10 or 100nM), a the vessel radius (12.5μm), F_0 the rate of chemokine uptake, and D the diffusion coefficient. The rate of chemokine uptake by the endothelial cells was estimated in the range of 1,000 to 10,000 molecules/cell/min by comparison with endocytosis rates for other proteins (Schwartz, Annu Rev Immunol 1990). A value of 0.6×10^{-7} cm^2/s for diffusion coefficient of the CINC-1 (MW 7,800) in the mesentery was interpolated from the diffusion coefficient of albumin (MW 66,000) determined experimentally in similar tissues (Parameswaran et al, Microcirculation 1999).

Results

In order to examine whether neutrophils were capable of bi-directional migration continuous gradients of IL-8 of varying steepness in microfabricated devices were established as previously described (Li Jeon, N., et al., (2002) Nat Biotechnol. 20(8):826-30). Previous work with microfabricated devices demonstrated robust chemotaxis of primary human neutrophils in gradients of

recombinant human IL-8 between 0 and 50nM and 0 and 100nM (Li Jeon, N., et al., (2002) Nat Biotechnol. 20(8):826-30). Since it had been previously demonstrated that T-cell undergoes fugetaxis at higher concentrations of the chemokine, SDF-1, gradients from 0 to 12nM, 0 to 120 nM, 0 to 1.2μM and 0 to 2.4 μM for IL-8 were further examined. Each gradient was initially calibrated and characterized as shown in Figures 10A through D and as previously described (Li Jeon, N., et al., (2002) Nat Biotechnol. 20(8):826-30). The differential concentration of chemokine across the migration channel ranged between 0.0267nM per micron to 5.34nM per micron or the equivalent of a difference in concentration of the chemokine of 0.267nM or 50.34 nM across the length of a 10 micron long neutrophil. Neutrophils were also exposed to control conditions including no chemokine or uniform concentrations of IL-8 of 12nM, 120nM or 1.2μM in the migration channel. Human neutrophils were loaded into the device and their migration tracked and quantitated using MetaMorph software in conjunction with MatLab software, respectively (Figures 10E through H). The initial and final density of cells across the migration channel was plotted for each of the conditions and the angular frequency of all directional movements determined for each cell using MetaMorph (Figures 10I through L). Cells exposed to no chemokine or chemokine at a uniform concentration across the migration channel underwent chemokinesis characterized by angular frequencies in all directions. In contrast, cells placed in gradients between 0 and 12nM and 0 and 120nM predominantly demonstrated chemotaxis with predominant angular frequencies occurring towards the peak concentration of the chemokine in the gradient (Figures 10M through P). Surprisingly, when cells were exposed to the steepest chemokine gradient of 0 to 1.2μM migratory behaviors were more complex. Cells in the lower third of the gradient chemotaxed towards higher levels of the chemokine whereas cells originating in the upper third of the gradient underwent fugetaxis down the gradient and away from the peak concentration of chemokine. Cells initially commencing at a position in the central third of the gradient underwent chemokinesis. The cell density across the migration channel prior to and after neutrophil migration reflects a redistribution of randomly arranged cells to the central third of this gradient (Figure 10L). In addition, the angular frequency distribution for this gradient reflects a predominant movement away from the

chemokine in this gradient (Figure 10P). Cells exposed to the steepest chemokine gradient studied, (0 to 2.4μM) underwent chemokinesis regardless of their position within the gradient (data not shown). In this way, the robust bi-directional neutrophil migration within a steep and temporally and spatially stable gradient of IL-8 was observed.

Further, videos of cells migrating in IL-8 gradients were analysed using MetaMorph software and each position of each cell in each frame was defined by its Cartesian coordinates within that frame. It was therefore possible to examine quantitative parameters which describe each cells migratory path. A random walk mode was used to quantitate cell migration , and the previously defined parameters of mean speed, random motility coefficient and persistence time to measure how "diffusive" or "ballistic" cell migration is and mean chemotropism index to measure the directionality of movement towards or away from a chemokine were used. Mean velocity and mean squared displacement for cells migrating in the absence of a chemokine or within gradients in which chemotaxis (0 to 12nM and 0 to 120nM) or fugetaxis (0 to 1.2μM) is seen predominantly (Figure 11A and11B). Measurement of mean velocity demonstrates that cells undergoing chemotaxis in the 0 to 120nM gradient or fugetaxis in the 0 to 1.2μM gradient migrate at similar speeds. Mean squared displacement reflects the directional bias of the cells random walk. Chemotaxing and fugetaxing cells demonstrate an exponentially increasing directional bias as they migrate in the 0 to 120nM and 0 to 1.2μM gradients, respectively. The gradient of the linear section of the mean squared displacement plot for cells migrating in each experimental and control condition defines the random motility coefficient for cell migration (Figure 15,Table 8). Random motility coefficients are significantly higher in cells undergoing directional migration in the 0 to 120nM and 0 to 1.2μM gradient than in the presence of a uniform concentration of IL-8 of 120nM in which chemokinesis predominates. The y-intercept of the linear segment of the mean squared displacement plot indicates the persistence time which is a measurement of how "ballistic" cell movement is (Figure 15,Table 8). The persistence time for cells migrating in linear gradients of varying steepness are greater than those for cells presented with no chemokine or a uniform concentration of chemokine. Persistence times for cell movement in the IL-8 gradient in which

chemotaxis (21.5 minutes) or fugetaxis (10.9 minutes) are seen predominantly are higher than those seen for cells undergoing chemokinesis in the absence of a gradient (0 minutes) or a uniform concentration of IL-8 (4.5 minutes). Chemotaxis and fugetaxis up or down a defined IL-8 gradient approach "ballistic" movement whereas cell movement in the absence of a chemokine gradient is more "diffusive".

The analysis of cell displacement within a random walk model of cell migration does not measure the directionality of movement towards or away from a chemokine. In addition, treating all cells equally within a gradient assumes that all cells behave in the same way in the same gradient. Since it had been identified that cells can migrate up or down a gradient in a manner that is dependent on their precise position within the gradient, the measurement of mean chemotropism index (MCI) was utilized to define the directionality of movement up (positive values) or down (negative values) a gradient and analysed cell movement three arbitrary sectors of each gradient (Figure 15, Table 8). Cells exposed to uniform concentrations of chemokine at 120nM or no chemokine had MCI values of -0.02 +/- 0.01 and 0.00 +/- 0.02 respectively. Cells undergoing chemotaxis in gradients between 0 and 12nM and 0 and 120nM demonstrated MCIs of +0.32 and + 0.39 respectively. In contrast, cells exposed to the steeper gradient of 0 to 1.2μM demonstrated a negative MCI of -0.13 supporting the view that the predominant movement of cells in the gradient was away from the peak concentration of IL-8. Cells migrating in the steepest 0 to 2.4μM gradient exhibited chemokinesis. In order to further analyse the effect of the influence of both gradient steepness and absolute concentration of the chemokine gradient each gradient was divided into three equal segments and cell populations, and commencing movement in each segment were then analysed separately. Cells migrating in all sectors of the 0 to 12nM and 0 to 120nM gradient reveal positive MCIs of between +0.21 and +0.44. Whereas, cells migrating in the lower segment of the 0 to 1.2μM gradient had a mean sectional MCI of +0.2, cells in the middle third and upper third of the gradient have negative MCIs of - 0.14 and - 0.22 respectively. These quantitative data which examine both the bias and direction of the random walk confirm the finding of bi-directional neutrophil migration. In addition, these quantitative data confirm that the directional decision of a cell to move up or down a gradient is determined by both the steepness

of the gradient and the absolute concentration of the chemokine that it is exposed to within the gradient.

Since receptor occupancy is known to play a role in directional decision making and gradient sensing in the context of chemotaxing eukaryotic cells, it was postulated that chemokine receptor occupancy by a chemokine might also play a critical role in the decision of a cell to move up or down a chemokine gradient. Thus, a SB25002, the specific non-peptide antagonist of the IL-8 receptor, CXCR2 was utilized to examine this postulate. Neutrophils were pretreated with SB225002 at concentrations between 1pM and 1μM and then exposed to 0 to 1.2μM gradients of IL-8 in microfabricated devices as described above. Videos of cell migration were analysed using MetaMorph and MathLab software to generate normalized angular frequencies determined for cells migrating in each of the three sectors of the gradient. The absence of inhibitor generates a normalized angular frequency of 1.0 whereas inhibition of fugetactic or chemotactic angular frequencies results in a normalized frequency of < 1.0 and augmentation of either directional response results in a value greater than 1. This analysis allows to precisely quantitate the effect of a given concentration of inhibitor on the directional decision of the cell to move up or down a gradient. The lowest concentrations of SB225002 (1pM and 100pM) lead to significant inhibition ($p = 0.0037$ and 0.0210) of fugetaxis whereas chemotaxis was infact augmented under these conditions (Figure 12). Gradually increasing concentrations of SB225002 ultimately inhibited both fugetaxis and chemotaxis. These data indicate that receptor occupancy plays a significant role in determining the directional decision of a cell to move up or down a steep IL-8 gradient. Furthermore, although IL-8 binds to both CXCR2 and CXCR1 on the cell surface, of the human neutrophil bi-directional signaling was evidently critically dependent on CXCR2.

It had been previously shown that the signaling pathway for chemotaxis is distinct from that for chemorepulsion or fugetaxis. It is known that T-cell fugetaxis in response to SDF-1 in standard transmigration assays was differentially more sensitive to inhibition by the intracytoplasmic cyclic nucleotide agonist 8-Br-cAMP than chemotaxis. Furthermore, it had been demonstrated that T-cell chemotaxis was differentially more sensitive to inhibition by the tyrosine kinase inhibitor, genistein, than was fugetaxis. The study of neutrophil migration in microfabricated devices

allows to examine precisely the effects of these inhibitors on quantitative parameters of cell migration including the directional bias of cells in the context of precisely defined and stable chemokine gradients. Primary human neutrophils were pretreated with known inhibitors of the chemokine signal transduction pathway including pertussis toxin, wortmannin, genistein, 8-Br-cAMP and 8-Br-cGMP and then exposed to IL-8 gradients in which chemotaxis and fugetaxis were seen. The effect of the inhibitor on directional migration towards or away from the chemokine was quantitated by determining the directional motility index of cells migrating in the context of these gradients. Movement vector angles corresponding to movement up the gradient (30 to 150 degrees - see Figure 13) were defined as chemotactic and measured movement vector angles corresponding to movement down the gradient (210 to 330 degrees - see figure) were defined as fugetactic. The directional choice of cells to move up or down a chemokine gradient were therefore compared in the presence and the absence of an inhibitor. Active movement with selective inhibition of directional sensing is manifest as an inverse relationship in distribution of angular frequencies between fugetactic and chemotactic sectors; if fugetaxis is inhibited (<1) chemotaxis will be augmented above normal (>1). Abrogation of directional sensing is manifest as a decrease of angular frequency distributions in both sectors towards zero. In this way it was demonstrated that both neutrophil chemotaxis and fugetaxis was significantly inhibited by pertussis toxin ($p = 0.007$ and $p = 0.003$ respectively). 8-Br-cAMP also selectively inhibited fugetaxis ($p = 4.6 \times 10^{-6}$) while the same concentration of this intracytoplasmic nucleotide agonist augmented chemotaxis ($p = 0.0008$). Wortmannin pretreatment of cells prior to placement in the 0 to 120nM or 0 to 1.2μM gradient generated more complex results than expected. Wortmannin significantly inhibited chemotaxis ($p = 0.0020$) and augmenting fugetaxis ($p = < 0.0001$) in the 0 to 120nM gradient and in contrast to this significantly augmenting chemotaxis ($p < 0.0001$) and inhibiting fugetaxis ($p < 0.0001$) in the context of the 0 to 1.2μM IL-8 gradient.

Further, the differential sensitivities of neutrophil chemotaxis and fugetaxis to wortmannin and 8-Br-cAMP were demonstrated. Both PI3K and cAMP have been shown to play a significant role in gradient sensing and directional decision making in eukaryotic cells including Dictyostelium, neutrophils, neurons and T-cells. It was also demonstrated that intracytoplasmic cAMP levels differentially

inhibit fugetaxis or chemorepulsion which is consistent with previous findings in eukaryotic neurons and T-cells. Wortmannin system inhibited the predominant direction of movement observed under control conditions in the gradient and augments the contrary directional decision which was not previously predominantly seen under control conditions. The distribution of PI3K and PTEN to the leading or trailing edge of the cell is thought to play a critical role in directional decision making in the context of eukaryotic cell chemotaxis. Chemotaxis is downregulated in the context of wortmannin in the shallow 0 to 120nM gradient as expected but surprisingly fugetaxis is augmented. When fugetaxis is inhibited by wortmannin in the steeper IL-8 gradient chemotaxis is augmented. This data supports previous work indicating a PI3K independent pathway governing the directional decision of neutrophils and that indicates that the leading and trailing edges can be interchangeable and that the localization of PI3K and or a second protein or proteins such as PTEN can determine the directional decision in the absence of PI3K activity.

Having demonstrated robust bi-directional migration of neutrophils to a defined IL-8 gradient *in vitro*, this observation was confirmed *in vivo*. Neutrophil migratory responses to the IL-8 orthologue, cytokine induced neutrophil chemoattractant-1 (CINC-1,) was evaluated in a rat model. CINC-1 and IL-8 are known and potent chemoattractants for murine neutrophils and signal migration via CXCR2. Rat CINC-1, unlike rat IL-8 has been cloned and is commercially available. Diffusive chemokine gradients were established in tissues adjacent to venules in mesentery which has been exteriorized in anesthetized animals. Diffusive gradients with peak concentrations adjacent to the point of superfusion and declining towards the venule as a result of adsorption of chemokine by matrix proteins, binding of chemokine to receptor and internalization of chemokine/receptor complexes and representation of chemokine on the luminal surface of endothelial cells. Chemokine gradients can be mathematically modeled in this context on the basis of predicable absorption and diffusion rates of the chemokine through tissue (Figures 14A through C). It is important to note that this gradient model predicts that the gradient shape between the source of chemokine superfusion and vessel wall is the same shape for all peak chemokine concentrations. The steepness of the gradient at any fixed point between the superfused chemokine and the vessel wall will therefore remain constant while the absolute concentration of chemokine seen at

that point varies. The *in vivo* model therefore proves to be of use in determining the effect of gradient steepness and absolute concentration on the directional decision of cells *in vivo*.

Two types of experiments were established in this model. First, mesenteric tissue adjacent to a venule was superfused with chemokine at a fixed concentration of 1nM, 10nM or 100nM for 90 minutes. Neutrophil migration was subsequently recorded by time lapse video microscopy and migrating neutrophils positively identified as such by subsequent acridine orange staining (Figure 14D). Under these conditions, peak transendothelial migration of neutrophils from the blood occurred towards peak concentrations of the chemokine of 10nM. Concentrations of 1nM lead to minimal neutrophil adhesion to the luminal surface of the venule and transmigration and concentrations of 100nM lead to accumulation of neutrophils around the vessel without transmigration towards the peak concentrations of CINC-1 (data not shown). In the second set of experiments the application of a chemokine gradients with a peak concentration of 10 nM (Figures 14E and Video 6) or 100nM for 45 minutes was replaced sequentially by a gradient with a peak concentration of 100nM (Figure 14F and Video 7) or 10nM in order to replace a potentially chemotactic gradient with a fugetactic gradient. Cell migration was tracked as previous described using MetaMorph software (Figure 14I).

Cells were observed undergoing chemotaxis out of the mesenteric venule towards peak concentrations of chemokine of 10nM in adjacent tissues as previously described (Figure 12H). However, in contrast, when a gradient with a peak concentration at the point of superfusion of 100nM replaced the previous lower concentration of chemokine, neutrophils were observed to migrate back towards the mesenteric venule (Figure 14I). Directional movement up or down a gradient was quantitated as previously described for cells migrating in defined gradients in vitro. Cell velocities and random motility coefficients of neutrophils migrating under these gradient conditions in vivo towards or away from peak concentrations of chemokine of 10nM and 100nM varied between 7.70 and 7.87 μm per minute and 64.57 to 135.11 μm^2/min (Figure 16, Table 9). These velocities and random motility coefficients were not significantly different from those seen for cell migrating in the gradients of similar steepness and absolute concentration of chemokine *in vitro* and varied between 2.0 and 5.1 microns/minute and between 504.11 and 831.33

μm^2/min. Interestingly persistence times for cells migrating *in vivo* were significantly less in vivo (2.31 to 5.25 min) than those seen in *vitro* (11.1 to 14.6 min) in gradients with peak concentrations of 10nM and 100nM and 12 nM and 120nM, respectively and may reflect the complexity of the surface over which the cells migrate in vivo as compared to the in vitro setting. Finally quantitative measurement of the directional bias of cells in gradients in *vivo*, including mean chemotropism index indicated that cells predominantly migrate towards a diffusive gradient of CINC-1 with a peak concentration of 10nM with MCI of +0.32 +/- 0.06 whereas cells moved away when this gradient was replaced with a gradient with a peak concentration of 100nM CINC-1 with a MCI of -0.35 +/- 0.12.

Conclusions

The *in vitro* and *in vivo* presented above rigorously demonstrate the ability neutrophils to move up or down a chemokine gradient. In contrast to the current paradigm, which argues that neutrophils only enter tissues as a result of positive chemitocatic agents, these findings indicate the existence of neutrophil chemorepellents which actively exclude neuttrophils form heathy uninfected tissues. Ultimately, these findings raise the possibility for the design of a novel class of anti-inflammatory agents which actively repel neutrophils from specific anatomic sites.

Equivalents

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by examples provided, since the examples are intended as a single illustration of one aspect of the invention and other functionally equivalent embodiments are within the scope of the invention. Various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims. The advantages and objects of the invention are not necessarily encompassed by each embodiment of the invention.

What is claimed is:

1. A method for identifying a nucleic acid expressed in a concentration dependent manner, comprising:

determining a first nucleic acid expression profile of a first cell at a first position in an agent concentration gradient,

determining a second nucleic acid expression profile of a second cell at a second position in the agent concentration gradient,

determining a difference between the first and second nucleic acid expression profiles,

wherein the first position in the agent concentration gradient corresponds to a first concentration of agent, and the second position in the agent concentration gradient corresponds to a second concentration of agent, and at least the second cell has migrated through the agent concentration gradient.

2. The method of claim 1, wherein the nucleic acid expression profile is an mRNA expression profile.

3. The method of claim 1, wherein the agent concentration gradient is a ligand concentration gradient.

4. The method of claim 1, wherein the agent concentration gradient is a chemokine concentration gradient.

5. The method of claim 4, wherein the chemokine concentration gradient is selected from the group consisting of SDF-1α, SDF-1β, IP-10, MIG, GROα, GROβ, GROγ, IL-8, PF4, MCP, MIP-1α, MIP-1β, MIP-1γ (mouse), MCP-2, MCP-3, MCP-4, MCP-5 (mouse), RANTES, fractalkine, lymphotactin, CXC, IL-8, GCP-2, ENA-78, NAP-2, IP-10, MIG, I-TAC, SDF-1α, BCA-1, PF4, Bolekine, HCC-1, Leukotactin-1 (HCC-2, MIP-5), Eotaxin, Eotaxin-2 (MPIF2), Eotaxin-3 (TSC), MDC, TARC, SLC (Exodus-2, 6CKine), MIP-3α (LARC, Exodus-1), ELC (MIP-3β), I-309, DC-CK1 (PARC, AMAC-1), TECK, CTAK, MPIF1 (MIP-3), MIP-5 (HCC-2), HCC-4 (NCC-4), C-10 (mouse), C Lymphotactin, and CX_3C Fracktelkine (Neurotactin) and ITAC concentration gradients.

6. The method of claim 3, wherein the agent concentration gradient is a cytokine concentration gradient.

7. The method of claim 6, wherein the cytokine concentration gradient is selected from the group consisting of PAF, N-formylated peptides, C5a, LTB_4 and

LXA_4, CXC, IL-8, GCP-2, GRO, GROα, GROβ, GROγ, ENA-78, NAP-2, IP-10, MIG, I-TAC, SDF-1α, BCA-1, PF4, Bolekine, MIP-1α, MIP-1β, RANTES, HCC-1, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5 (mouse), Leukotactin-1 (HCC-2, MIP-5), Eotaxin, Eotaxin-2 (MPIF2), Eotaxin-3 (TSC), MDC, TARC, SLC (Exodus-2, 6CKine), MIP-3α (LARC, Exodus-1), ELC (MIP-3β), I-309, DC-CK1 (PARC, AMAC-1), TECK, CTAK, MPIF1 (MIP-3), MIP-5 (HCC-2), HCC-4 (NCC-4), MIP-1γ (mouse), C-10 (mouse), C Lymphotactin, and CX_3C Fracktelkine (Neurotactin), SDF-1α, SDF-1β, met-SDF-1β, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-10, IL-12, IL-15, IL-18, TNF, IFN-α, IFN-β, IFN-γ, granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), macrophage colony stimulating factor (M-CSF), TGF-β, FLT-3 ligand, VEGF, DMDA, endothelin and CD40 ligand concentration gradients.

8. The method of claim 1, wherein the first concentration of agent is a zero concentration of agent, and the second concentration of agent is a non-zero concentration of agent.

9. The method of claim 1, wherein the first concentration of agent is greater than the second concentration of agent.

10. The method of claim 1, wherein the first cell has migrated through the agent concentration gradient.

11. The method of claim 1 or 10, wherein migration through the agent concentration gradient is fugetactic migration.

12. The method of claim 1 or 10, wherein migration through the agent concentration gradient is chemotactic migration.

13. The method of claim 1, wherein the nucleic acid expression profile is determined by Northern analysis.

14. The method of claim 1, wherein the nucleic acid expression profile is determined by polymerase chain reaction (PCR) analysis.

15. The method of claim 1, wherein the nucleic acid expression profile is determined by nucleic acid chip analysis.

16. The method of claim 1, wherein the gradient is a step gradient.

17. The method of claim 1, wherein the gradient is a continuous gradient.

18. The method of claim 1, wherein the gradient comprises a second gradient co-existing with the first gradient.

19. The method of claim 1, wherein the first and second cells are adult cells.

20. The method of claim 1, wherein the first and second cells are human cells.

21. The method of claim 1, wherein the first and second cells are primary cells.

22. The method of claim 1, wherein the first and second cells are hemopoietic cells.

23. The method of claim 1, wherein the first and second cells are T lymphocytes.

24. The method of claim 1, wherein the first and second cells are neural cells.

25. A method for identifying a compound that can modulate cell migration in one or more agent concentration gradients comprising:

contacting a migratory cell in an agent concentration gradient with a test compound;

determining the nucleic acid expression profile in the cell; and

identifying a change in expression of a gene expression product.

26. The method of claim 25, wherein the cell migration is chemotaxic migration and the gene expression product is a chemotactic specific gene expression product.

27. The method of claim 25, wherein the cell migration is fugetaxic migration and the gene expression product is a chemotactic specific gene expression product.

28. The method of claim 25, wherein the nucleic acid expression profile is an mRNA expression profile.

29. The method of claim 25, wherein the agent concentration gradient is a ligand concentration gradient.

30. The method of claim 25, wherein the agent concentration gradient is a chemokine concentration gradient.

31. The method of claim 30, wherein the chemokine concentration gradient is selected from the group consisting of SDF-1α, SDF-1β, IP-10, MIG, GROα, GROβ, GROγ, IL-8, PF4, MCP, MIP-1α, MIP-1β, MIP-1γ (mouse), MCP-2, MCP-3, MCP-4, MCP-5 (mouse), RANTES, fractalkine, lymphotactin, CXC, IL-8, GCP-2, ENA-78, NAP-2, IP-10, MIG, I-TAC, SDF-1α, BCA-1, PF4, Bolekine,

HCC-1, Leukotactin-1 (HCC-2, MIP-5), Eotaxin, Eotaxin-2 (MPIF2), Eotaxin-3 (TSC), MDC, TARC, SLC (Exodus-2, 6CKine), MIP-3α (LARC, Exodus-1), ELC (MIP-3β), I-309, DC-CK1 (PARC, AMAC-1), TECK, CTAK, MPIF1 (MIP-3), MIP-5 (HCC-2), HCC-4 (NCC-4), C-10 (mouse), C Lymphotactin, and CX_3C Fracktelkine (Neurotactin) and ITAC concentration gradients.

32. The method of claim 25, wherein the agent concentration gradient is a cytokine concentration gradient.

33. The method of claim 32, wherein the cytokine concentration gradient is selected from the group consisting of the cytokine concentration gradient is selected from the group consisting of PAF, N-formylated peptides, C5a, LTB_4 and LXA_4, CXC, IL-8, GCP-2, GRO, GROα, GROβ, GROγ, ENA-78, NAP-2, IP-10, MIG, I-TAC, SDF-1α, BCA-1, PF4, Bolekine, MIP-1α, MIP-1β, RANTES, HCC-1, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5 (mouse), Leukotactin-1 (HCC-2, MIP-5), Eotaxin, Eotaxin-2 (MPIF2), Eotaxin-3 (TSC), MDC, TARC, SLC (Exodus-2, 6CKine), MIP-3α (LARC, Exodus-1), ELC (MIP-3β), I-309, DC-CK1 (PARC, AMAC-1), TECK, CTAK, MPIF1 (MIP-3), MIP-5 (HCC-2), HCC-4 (NCC-4), MIP-1γ (mouse), C-10 (mouse), C Lymphotactin, and CX_3C Fracktelkine (Neurotactin), SDF-1α, SDF-1β, met-SDF-1β, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-10, IL-12, IL-15, IL-18, TNF, IFN-α, IFN-β, IFN-γ, granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), macrophage colony stimulating factor (M-CSF), TGF-β, FLT-3 ligand, VEGF, DMDA, endothelin and CD40 ligand concentration gradients.

34. The method of claim 25, wherein the nucleic acid expression profile is determined at two different concentrations of agent.

35. The method of claim 34, wherein the two different concentrations of agent are a zero concentration of agent and a non-zero concentration of agent.

36. The method of claim 35, wherein the cell at a zero concentration of gradient has migrated through a gradient.

37. The method of claim 25, wherein the nucleic acid expression profile is determined by Northern analysis.

38. The method of claim 25, wherein the nucleic acid expression profile is determined by polymerase chain reaction (PCR) analysis.

39. The method of claim 25, wherein the nucleic acid expression profile is determined by nucleic acid chip analysis.

40. The method of claim 25, wherein the gradient is a step gradient.

41. The method of claim 25, wherein the gradient is a continuous gradient.

42. The method of claim 25, wherein the gradient comprises a second gradient co-existing with the first gradient.

43. The method of claim 25, wherein the cell is an adult cell.

44. The method of claim 25, wherein the cell is a human cell.

45. The method of claim 25, wherein the cell is a primary cell.

46. The method of claim 25, wherein the cell is a hemopoietic cell.

47. The method of claim 25, wherein the cell is a T lymphocyte.

48. The method of claim 25, wherein the cell is a neural cell.

49. A method for inhibiting cell fugetaxis comprising

contacting a cell undergoing or likely to undergo fugetaxis with an agent that inhibits a fugetaxis specific gene expression product in an amount effective to inhibit fugetaxis.

50. The method of claim 49, wherein the fugetaxis specific gene expression product is a nucleic acid or a peptide.

51. The method of claim 49, wherein the fugetaxis specific gene expression product is a signaling molecule.

52. The method of claim 49, wherein the signaling molecule is selected from the group consisting of cell division cycle 42, annexin A3, Rap1 guanine nucleotide exchange factor, adenylate cyclase 1, JAK binding protein, and Rho GDP dissociation inhibitor alpha.

53. The method of claim 52, wherein the signaling molecule is selected from the group consisting of cell division cycle 42 (cdc42), ribosomal protein S6 kinase, BAI1-associated protein 2, GTPase regulator associated with FAK, protein kinase C-beta 1, phosphoinositide-specific phospholipase C-beta 1, nitric oxide synthase 1, phosphatidylinositol-4-phosphate 5-kinase, and MAP kinase kinase kinase kinase 4.

54. The method of claim 49, wherein the fugetaxis specific gene expression product is a extracellular matrix related molecule.

55. The method of claim 54, wherein the extracellular matrix related molecule is selected from the group consisting of chitinase 3-like 1 (cartilage glycoprotein-39), carcinoembryonic antigen-related cell adhesion molecule 6, matrix metalloproteinase 8 (neutrophil collagenase), integrin cytoplasmic domain-associated protein 1, ficolin (collagenfibrinogen domain-containing) 1, epithelial V-like antigen 1, vascular endothelial growth factor (VEGF), fibulin 1, carcinoembryonic antigen-related cell adhesion molecule 3, and lysosomal-associated membrane protein 1.

56. The method of claim 49, wherein the fugetaxis specific gene expression product is a cytoskeleton related molecule.

57. The method of claim 56, wherein the cytoskeleton related molecule is selected from the group consisting of ankyrin 1 (erythrocytic), S100 calcium-binding protein A12 (calgranulin C), plectin 1 (intermediate filament binding protein, 500kD), microtubule-associated protein RPEB3, microtubule-associated protein 1A like protein (MILP), capping protein (actin filament, gelsolin-like), and ankyrin 2 (neuronal).

58. The method of claim 49, wherein the fugetaxis specific gene expression product is a cell cycle molecule.

59. The method of claim 58, wherein the cell cycle molecule is selected from the group consisting of v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog, lipocalin 2 (oncogene 24p3), lectin, (galactoside-binding, galectin 3), RAB31 (member RAS oncogene family), disabled (Drosophila) homolog 2 (mitogen-responsive phosphoprotein), RAB9 (member RAS oncogene family, pseudogene 1), and growth differentiation factor 8.

60. The method of claim 49, wherein the fugetaxis specific gene expression product is an immune response related molecule.

61. The method of claim 61, wherein the immune response related molecule is selected from the group consisting of major histocompatibility complex (class II, DR alpha), S100 calcium-binding protein A8 (calgranulin A), small inducible cytokine subfamily A (Cys-Cys), eukaryotic translation initiation factor 5A, small inducible cytokine subfamily B (Cys-X-Cys) (member 6, granulocyte chemotactic protein 2), Fc fragment of IgG binding protein, CD24 antigen (small cell lung carcinoma cluster 4 antigen), MHC class II transactivator, T cell receptor

(alpha chain), T cell activation (increased late expression), MKP-1 like protein tyrosine phosphatase, T cell receptor gamma constant 2, T cell receptor gamma locus, cytochrome P450 (subfamily IVF, polypeptide 3, leukotriene B4 omega hydroxylase).

62. The method of claim 49, wherein the cell is an immune cell.

63. The method of claim 49, wherein the contacting occurs in vivo in a subject having or at risk of having an abnormal immune response.

64. The method of claim 49, wherein the cell is a neural cell.

65. The method of claim 49, wherein the fugetaxis specific gene expression product is chemokine (C-X3-C) receptor 1.

66. A method for inhibiting cell chemotaxis comprising

contacting a cell undergoing or likely to undergo chemotaxis with an agent that inhibits a chemotaxis specific gene expression product in an amount effective to inhibit chemotaxis.

67. The method of claim 66, wherein the chemotaxis specific gene expression product is a nucleic acid or a peptide.

68. The method of claim 66, wherein the cell is a immune cell.

69. The method of claim 66, wherein the contacting occurs in vivo in a subject having or at risk of having an abnormal immune response.

70. The method of claim 66, wherein the abnormal immune response is an inflammatory response.

71. The method of claim 66, wherein the abnormal immune response is an autoimmune response.

72. The method of claim 71, wherein the autoimmune response is selected from the group consisting of rheumatoid arthritis, Crohn's disease, multiple sclerosis, systemic lupus erythematosus (SLE), autoimmune encephalomyelitis, myasthenia gravis (MG), Hashimoto's thyroiditis, Goodpasture's syndrome, pemphigus (e.g., pemphigus vulgaris), Grave's disease, autoimmune hemolytic anemia, autoimmune thrombocytopenic purpura, scleroderma with anti-collagen antibodies, mixed connective tissue disease, polymyositis, pernicious anemia, idiopathic Addison's disease, autoimmune-associated infertility, glomerulonephritis (e.g., crescentic glomerulonephritis, proliferative glomerulonephritis), bullous

pemphigoid, Sjögren's syndrome, insulin resistance, and autoimmune diabetes mellitus.

73. The method of claim 66, wherein the abnormal immune response is a graft versus host response.

74. The method of claim 66, wherein the chemotaxis specific gene expression product is a signaling molecule.

75. The method of claim 74, wherein the signaling molecule is selected from the group consisting of G protein-coupled receptor kinase 6, vaccinia related kinase 1, PTK2 protein tyrosine kinase 2, STAM-like protein containing SH3 and ITAM domains 2, signal-induced proliferation-associated gene 1, CD47 antigen (Rh-related antigen, integrin-associated signal transducer), and protein tyrosine phosphatase (non-receptor type 12).

76. The method of claim 74, wherein the signaling molecule is selected from the group consisting of PTK2 (focal adhesion kinase), MAP kinase kinase kinase kinase 2, guanine nucleotide binding protein, PT phosphatase (receptor), cdc42-binding protein kinase beta, Ral GEF (RalGPS1A), MAP kinase 7, autotaxin, inositol 1,4,5-triphosphate receptor, phosphoinositide-3-kinase gamma, PT phosphatase (non-receptor), RAS p21 protein activator (GAP), RAS guanyl releasing protein 2, and Arp23 complex 20kDa subunit.

77. The method of claim 66, wherein the chemotaxis specific gene expression product is a extracellular matrix related molecule.

78. The method of claim 77, wherein the extracellular matrix related molecule is selected from the group consisting of spondin 1 (f-spondin, extracellular matrix protein), collagen type XVIII (alpha 1), CD31 adhesion molecule, tetraspan 3, glycoprotein A33, and angio-associated migratory cell protein.

79. The method of claim 66, wherein the chemotaxis specific gene expression product is a cytoskeleton related molecule.

80. The method of claim 79, wherein the cytoskeleton related molecule is selected from the group consisting of actin related protein 23 complex (subunit 4, 20 kD), tropomyosin 2 (beta), SWISNF related matrix associated actin dependent regulator of chromatin (subfamily a, member 5), spectrin beta (non-erythrocytic 1), myosin light polypeptide 5 (regulatory), keratin 1, plakophilin 4, and capping protein (actin filament, muscle Z-line, alpha 2).

81. The method of claim 66, wherein the chemotaxis specific gene expression product is a cell cycle molecule.

82. The method of claim 81, wherein the cell cycle molecule is selected from the group consisting of FGF receptor activating protein 1, v-maf musculoaponeurotic fibrosarcoma (avian) oncogene homolog, cyclin-dependent kinase (CDC2-like) 10, TGFB inducible early growth response 2, retinoic acid receptor alpha, anaphase promoting complex subunit 10, RAS p21 protein activator (GTPase activating protein, 3-Ins-1,3,4,5, -P4 binding protein), cell division cycle 27, programmed cell death 2, c-myc binding protein, mitogen-activated protein kinase kinase kinase 1, TGF beta receptor III (betaglycan, 300 kDa), and G1 to S phase transition 1.

83. The method of claim 66, wherein the chemotaxis specific gene expression product is an immune response related molecule.

84. The method of claim 83, wherein the immune response related molecule is selected from the group consisting of major histocompatibility complex class II DQ beta 1, bone marrow stromal cell antigen 2, Burkitt lymphoma receptor 1 (GTP binding protein, CXCR5), CD7 antigen (p41), Stat2 type a, T cell immune regulator 1, and interleukin 21 receptor.

85. The method of claim 66, wherein the cell is a neural cell.

86. A method for promoting cell fugetaxis comprising

contacting a cell with a non-chemokine agent that promotes fugetaxis in an amount effective to promote fugetaxis.

87. The method of claim 86, wherein the contacting occurs in vivo in a subject having a disorder characterized by lack of fugetaxis.

88. The method of claim 86, wherein the cell is a hematopoietic cell.

89. The method of claim 88, wherein the hematopoietic cell is a T lymphocyte.

90. The method of claim 86, wherein the cell is a neural cell.

91. A method for promoting cell chemotaxis comprising

contacting a cell with a non-chemokine agent that promotes chemotaxis in an amount effective to promote chemotaxis.

92. The method of claim 91, wherein the contacting occurs in vivo in a subject having a disorder characterized by lack of chemotaxis.

93. The method of claim 91, wherein the cell is a hematopoietic cell.

94. The method of claim 93, wherein the hematopoietic cell is a T lymphocyte.

95. The method of claim 91, wherein the cell is a neural cell.

96. The method of claim 62 or 68, wherein the immune cell is a selected from the group consisting of T-cells, B-cells, NK cells, dendritic cells, monocytes and macrophages.

97. The method of claim 96, wherein the immune cell is an inflammatory selected from the group consisting of neutrophils, basophils, eosinophils and mast cells.

98. The method of claim 88 and 93, wherein the hematopoietic cell is an immune cell is a selected from the group consisting of T-cells, B-cells, NK cells, dendritic cells, monocytes and macrophages.

99. The method of claim 98, wherein the immune cell is an inflammatory selected from the group consisting of neutrophils, basophils, eosinophils and mast cells.

100. A method for promoting neutrophil chemotaxis comprising contacting a neutrophil with IL-8 in an amount effective to promote chemotaxis.

101. The method of claim 100, wherein the neutrophil is contacted with a low concentration of IL-8.

102. The method of claim 101, wherein the low concentration of IL-8 is between about 10 ng/ml to about 500 ng/ml.

103. The method of claim 100, wherein the contacting occurs in vivo in a subject having a disorder characterized by lack of neutrophil chemotaxis.

104. The method of claim 103, wherein the disorder is selected from the group consisting of bacterial infections and granulomatous diseases.

105. The method of claim 103, wherein IL-8 is provided to the subject on a material surface coated with IL-8.

106. The method of claim 105, wherein the material surface is implanted within the subject.

107. The method of claim 103, wherein IL-8 is provided to the subject in a controlled release formulation.

108. A method for promoting neutrophil fugetaxis comprising contacting a neutrophil with IL-8 in an amount effective to promote fugetaxis.

109. The method of claim 108, wherein the neutrophil is contacted wih a high concentration of IL-8.

110. The method of claim 109, wherein the concentration of IL-8 is between about 1 microgram/ml to about 10 micrograms/ml.

111. The method of claim 108, wherein the contacting occurs in vivo in a subject having a disorder characterized by lack of neutrophil fugetaxis.

112. The method of claim 111, wherein the disorder is selected from the group consisting of inflammatory or immune mediated diseases, rejection of a transplanted organ or tissue, rheumatoid arthritis, automimmune diseases and asthma.

113. The method of claim 108, wherein IL-8 is provided to the subject on a material surface coated with IL-8.

114. The method of claim 113, wherein the material surface is implanted within the subject.

115. The method of claim 108, wherein IL-8 is provided to the subject in a controlled release formulation.

116. A method for inhibiting IL-8 induced neutrophil chemotaxis comprising contacting a neutrophil with wortmannin in an amount effective to inhibit chemotaxis and optionally induce fugetaxis by the neutrophil.

117. A method for inhibiting IL-8 induced neutrophil fugetaxis comprising contacting a neutrophil with LY294002 in an amount effective to inhibit fugetaxis and optionally induce chemotaxis by the neutrophil.

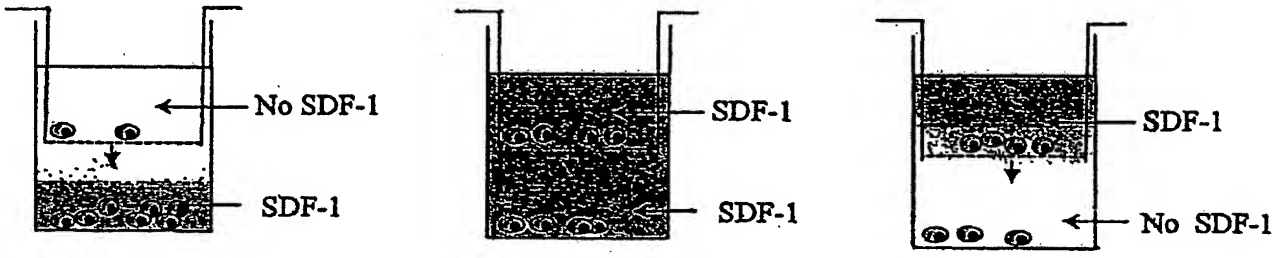
118. The method of claim 4 or 30, wherein the chemokine concentration gradient is a SDF-1 concentration gradient.

119. The method of claim 4 or 30, wherein the chemokine concentration gradient is an IL-8 concentration gradient.

120. The method of claim 6 or 32, wherein the cytokine concentration gradient is a SDF-1 concentration gradient.

121. The method of claim 6 or 32, wherein the cytokine concentration gradient is an IL-8 concentration gradient.

T-cell Transmigration Assays



Migration towards SDF-1 (chemotaxis)

Random movement in response to SDF-1 (chemokinesis)

Migration away from SDF-1 (fugetaxis)

FIGURE 1

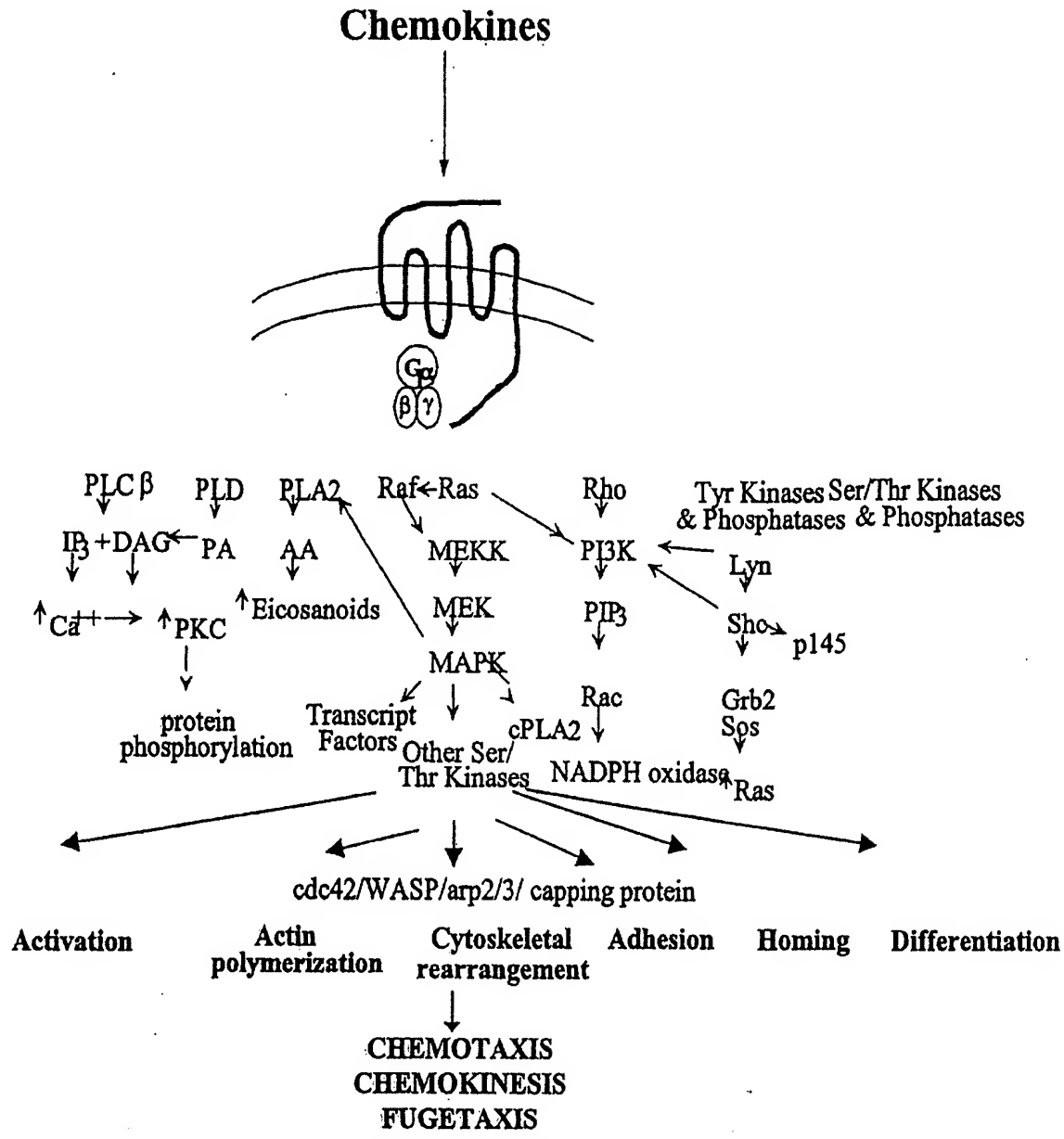


FIGURE 2A

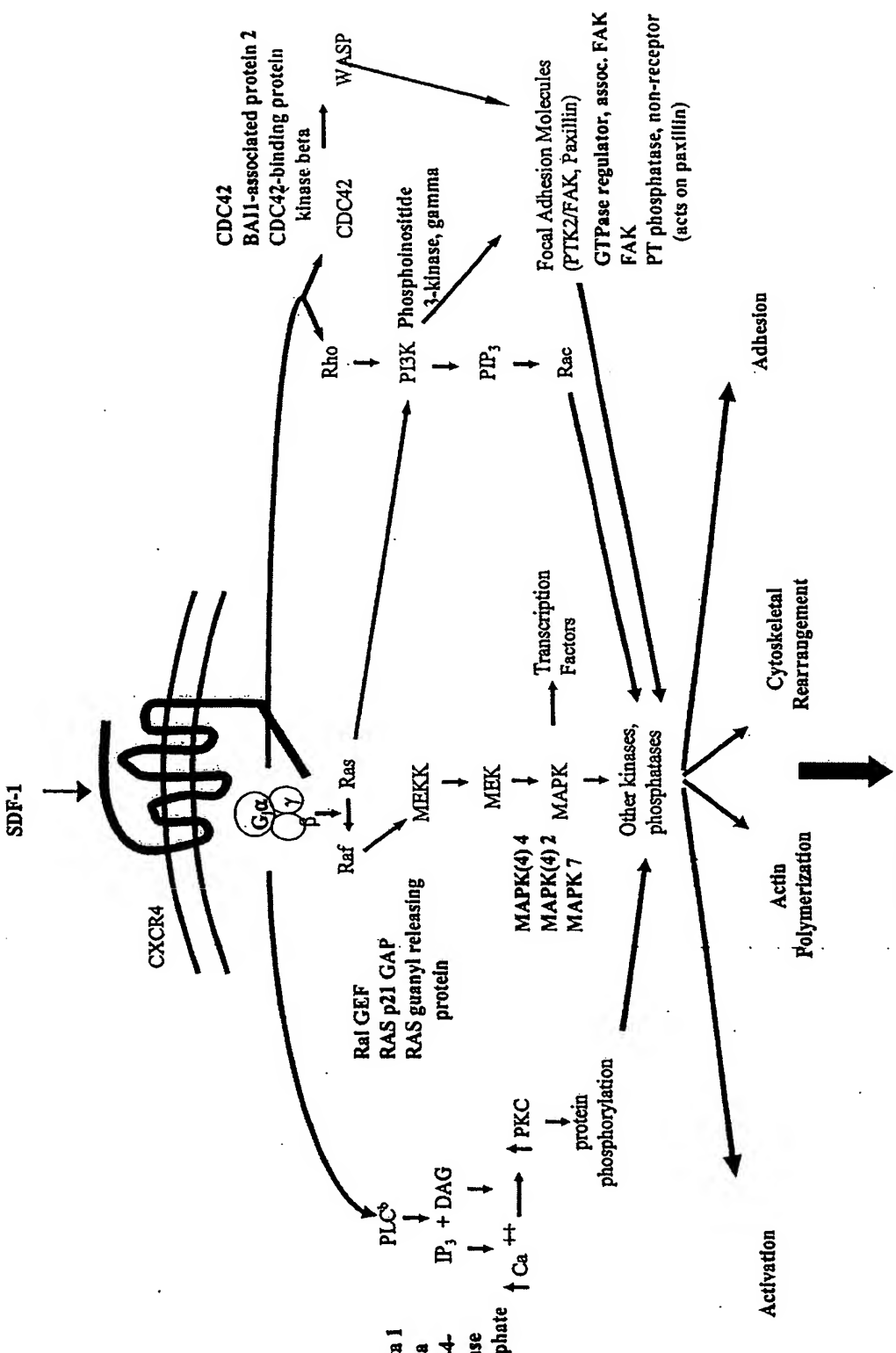

SDF-1
CXCR4
Gα
β
γ
Ras
Raf
MEKK
MEK
MAPK
MAPK(4) 4
MAPK(4) 2
MAPK 7
Ral GEF
RAS p21 GAP
RAS guanyl releasing protein
Rho
PI3K
Phospholnositide 3-kinase, gamma
PIP3
Rac
CDC42
BAI1-associated protein 2
CDC42-binding protein kinase beta
CDC42
WASP
Focal Adhesion Molecules (PTK2/FAK, Paxillin)
GTPase regulator, assoc. FAK
FAK
PT phosphatase, non-receptor (acts on paxillin)
Transcription Factors
Other kinases, phosphatases
Adhesion
Cytoskeletal Rearrangement
Actin Polymerization
MIGRATION
Activation
PLCβ
IP3 + DAG
↑Ca ++
↑PKC
protein phosphorylation
Protein kinase C, beta 1
Phospholipase C, beta
Phosphatidylinositol-4-phosphate 5-kinase
Inositol 1,4,5-triphosphate receptor

FIGURE 2B

FIGURE 3

Table 1
Differential Gene Expression in Chemokinesis vs Medium SDF-1 Gradients

UP REGULATED IN CHEMOKINESIS COMPARED TO MEDIUM SDF-1 GRADIENTS

8.54	Hs.223014 antizyme inhibitor
6.88	Hs.740 PTK2 protein tyrosine kinase 2
6.62	Hs.6891 splicing factor, arginineserine-rich 6
5.45	Hs.73172 growth factor independent 1
5.38	Hs.73931 major histocompatibility complex, class II, DQ beta 1
4.97	Hs.18895 tousled-like kinase 1
4.69	Hs.76536 transducin (beta)-like 1
3.95	Hs.158688 KIAA0741 gene product
3.89	Hs.82985 collagen, type V, alpha 2
3.73	Hs.7358 hypothetical protein FLJ13110
3.70	Hs.75231 solute carrier family 16 (monocarboxylic acid transporters), member 1
3.67	Hs.236646 homeo box D9
3.64	Hs.9701 growth arrest and DNA-damage-inducible, gamma
3.63	Hs.73793 vascular endothelial growth factor
3.62	gb:BC006233.1 /DEF=Homo sapiens, ketohexokinase (fructokinase), clone MGC:10370, mRNA, complete cds.
3.52	Hs.171814 parathymosin
3.45	Hs.2969 v-ski avian sarcoma viral oncogene homolog
3.39	Hs.321223 keratin 6B
3.33	Hs.139648 KIAA0706 gene product
3.32	Hs.66309 Homo sapiens, Similar to RIKEN cDNA 2310034L04 gene, clone MGC:11061, mRNA, complete cds
3.22	Hs.54505 aquaporin 6, kidney specific
3.13	Hs.84285 ubiquitin-conjugating enzyme E2I (homologous to yeast UBC9)
3.05	Hs.135626 chymase 1, mast cell
3.00	Hs.249216 H2B histone family, member J
3.00	Hs.288650 aquaporin 4
2.95	Hs.82085 serine (or cysteine) proteinase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1
2.93	Hs.287763 Human DNA sequence from clone RP1-23O21 on chromosome 6. Contains acidic calponin 3 (CNN3) pseudogene
2.92	Hs.322680 Homo sapiens cDNA: FLJ21547 fis, clone COL06206
2.91	Hs.301667 Homo sapiens mRNA; cDNA DKFZp566I043 (from clone DKFZp566I043)
2.90	gb:BC006114.1 /DEF=Homo sapiens, Similar to cholinergic receptor, nicotinic, alpha polypeptide 3, clone MGC:12991, mRNA
2.88	Hs.173594 serine (or cysteine) proteinase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 1
2.85	Hs.162200 urotensin 2
2.84	Hs.24385 Human hbc647 mRNA sequence
2.80	Hs.280380 aminopeptidase
2.75	Hs.25732 eukaryotic translation initiation factor 4 gamma, 3
2.70	Hs.79876 steroid sulfatase (microsomal), arylsulfatase C, isozyme S
2.66	Hs.306243 Homo sapiens thioredoxin delta 3 (TXN delta 3) mRNA, partial cds
2.64	Hs.2388 apolipoprotein F
2.63	Hs.292787 ESTs
2.62	Hs.34114 ATPase, Na+K+ transporting, alpha 2 (+) polypeptide
2.62	Hs.82065 interleukin 6 signal transducer (gp130, oncostatin M receptor)
2.62	Hs.271926 serologically defined colon cancer antigen 16
2.60	Hs.15791 transmembrane 7 superfamily member 1 (upregulated in kidney)
2.60	Hs.136075 Homo sapiens cDNA: FLJ23438 fis, clone HRC13275
2.55	Hs.121068 transmembrane 4 superfamily member 6
2.54	Hs.182740 ribosomal protein S11
2.53	Hs.82280 regulator of G-protein signalling 10
2.52	Hs.239114 mannosidase, alpha, class 1A, member 2
2.52	Hs.302022 PR domain containing 16
2.51	Hs.110903 claudin 5 (transmembrane protein deleted in velocardiofacial syndrome)

FIGURE 3

Table 1
Differential Gene Expression in Chemokinesis vs Medium SDF-1 Gradients

2.50	Hs.3005 transcription factor AP-4 (activating enhancer-binding protein 4)
2.50	Hs.293334 ESTs
2.49	Hs.66578 corticotropin releasing hormone receptor 2
2.46	Hs.286233 sperm autoantigenic protein 17
2.38	Hs.99971 zinc finger protein 272
2.34	Hs.24322 ATPase, H+ transporting, lysosomal (vacuolar proton pump) 9kD
2.34	Hs.154762 HIV-1 rev binding protein 2
2.32	Hs.84152 cystathionine-beta-synthase
2.31	Hs.96 phorbol-12-myristate-13-acetate-induced protein 1
2.31	Hs.247043 type 1 tumor necrosis factor receptor shedding aminopeptidase regulator
2.30	Hs.55481 zinc finger protein 165
2.29	Hs.8074 brain-specific angiogenesis inhibitor 3
2.29	Hs.103978 serinethreonine kinase 22B (spermiogenesis associated)
2.27	Hs.306618 Homo sapiens cDNA FLJ11930 fis, clone HEMBB1000441
2.26	Hs.194669 enhancer of zeste (Drosophila) homolog 1
2.26	Hs.16488 calreticulin
2.25	Hs.305979 Homo sapiens clone FLB3024 PRO0756 mRNA, complete cds
2.25	Hs.79170 KIAA0227 protein
2.23	Hs.306602 Homo sapiens cDNA FLJ11514 fis, clone HEMBA1002229
2.22	Hs.223241 eukaryotic translation elongation factor 1 delta (guanine nucleotide exchange protein)
2.21	Hs.79042 neuromedin B receptor
2.19	Hs.93304 phospholipase A2, group VII (platelet-activating factor acetylhydrolase, plasma)
2.19	Hs.247741 protocadherin alpha 2
2.19	Hs.16488 calreticulin
2.18	Hs.129928 KIAA0477 gene product
2.17	Hs.54481 low density lipoprotein receptor-related protein 8, apolipoprotein e receptor
2.17	Hs.133130 Homo sapiens mRNA; cDNA DKFZp566H0124 (from clone DKFZp566H0124)
2.17	Hs.306778 Homo sapiens cDNA: FLJ21524 fis, clone COL05921
2.16	Hs.239176 insulin-like growth factor 1 receptor
2.13	Hs.53973 vasoactive intestinal peptide
2.13	Hs.262869 plasminogen-like
2.12	Hs.86958 interferon (alpha, beta and omega) receptor 2
2.09	Hs.86368 calmegin
2.07	Hs.169488 dentatorubral-pallidoluysian atrophy (atrophin-1)
2.07	Hs.21838 hypothetical protein FLJ11191
2.07	Hs.28777 H2A histone family, member L
2.05	Hs.199538 inhibin, beta C
2.05	Hs.272529 glycosylphosphatidylinositol specific phospholipase D1
2.05	Hs.248999 ESTs
2.04	Hs.39328 /len=463
2.04	Hs.287809 Human HOX-2.5 gene for homeodomain protein, partial
2.02	Hs.64639 glioma pathogenesis-related protein
2.02	Hs.274402 heat shock 70kD protein 1B
2.01	Hs.56145 thymosin, beta, identified in neuroblastoma cells
2.00	Hs.151641 glycoprotein A repetitions predominant
2.00	Hs.69547 myelin basic protein
1.97	Hs.180919 inhibitor of DNA binding 2, dominant negative helix-loop-helix protein
1.94	Hs.5327 PRO1914 protein
1.93	Hs.85302 adenosine deaminase, RNA-specific, B1 (homolog of rat RED1)
1.92	Hs.118786 metallothionein 2A
1.92	Hs.278572 anaplastic lymphoma kinase (Ki-1)
1.91	Hs.315463 suppression of tumorigenicity 16 (melanoma differentiation)
1.91	Hs.159526 patched (Drosophila) homolog

FIGURE 3

Table 1
Differential Gene Expression in Chemokinesis vs Medium SDF-1 Gradients

1.91	Hs.24322 ATPase, H+ transporting, lysosomal (vacuolar proton pump) 9kD
1.90	Hs.25732 eukaryotic translation initiation factor 4 gamma, 3
1.90	Hs.288771 DKFZP586A0522 protein
1.89	Hs.180919 inhibitor of DNA binding 2, dominant negative helix-loop-helix protein
1.89	Hs.42244 Homo sapiens mRNA; cDNA DKFZp564A023 (from clone DKFZp564A023)
1.89	Hs.82101 pleckstrin homology-like domain, family A, member 1
1.89	Hs.279582 GTP-binding protein Sara
1.84	Hs.306639 Homo sapiens cDNA FLJ12624 fis, clone NT2RM4001754
1.83	Hs.55075 KIAA0410 gene product
1.83	Hs.142023 T cell activation, increased late expression
1.83	Hs.180919 inhibitor of DNA binding 2, dominant negative helix-loop-helix protein
1.82	Hs.64639 glioma pathogenesis-related protein
1.80	Hs.48778 niban protein
1.79	Hs.36927 heat shock 105kD
1.79	Hs.4147 translocating chain-associating membrane protein
1.78	Hs.75574 mitochondrial ribosomal protein L19
1.78	Hs.135202 c-myc promoter-binding protein
1.78	Hs.298014 Homo sapiens cDNA FLJ14136 fis, clone MAMMA1002744
1.78	Hs.198267 mucin 4, tracheobronchial
1.78	Hs.113009 hypothetical protein FLJ22527
1.77	Hs.76064 ribosomal protein L27a
1.76	Hs.8786 carbohydrate (chondroitin 6keratan) sulfotransferase 2
1.76	Hs.75825 pleiomorphic adenoma gene-like 1
1.74	Hs.75825 pleiomorphic adenoma gene-like 1
1.72	Hs.26613 Homo sapiens mRNA; cDNA DKFZp586F1323 (from clone DKFZp586F1323)
1.71	Hs.3886 karyopherin alpha 3 (importin alpha 4)

FIGURE 3

Table 1
Differential Gene Expression in Chemokinesis vs Medium SDF-1 Gradients

DOWN REGULATED IN CHEMOKINESIS COMPARED TO MEDIUM SDF-1 GRADIENTS	
-8.38	Hs.12142 WD repeat domain 13
-8.19	Hs.279623 selenoprotein X, 1
-6.29	Hs.180577 granulin
-6.24	Hs.41 carcinoembryonic antigen-related cell adhesion molecule 8
-6.08	Hs.99863 elastase 2, neutrophil
-5.87	Hs.99960 membrane-spanning 4-domains, subfamily A, member 3 (hematopoietic cell-specific)
-5.22	Hs.286124 CD24 antigen (small cell lung carcinoma cluster 4 antigen)
-5.14	Hs.29417 HCF-binding transcription factor Zhangfei
-4.87	Hs.25817 BTB (POZ) domain containing 2
-4.87	Hs.193716 complement component (3b4b) receptor 1, including Knops blood group system
-4.75	Hs.10306 natural killer cell group 7 sequence
-4.56	Hs.26319 KIAA0833 protein
-4.54	Hs.300772 tropomyosin 2 (beta)
-4.49	Hs.457 fucosyltransferase 7 (alpha (1,3) fucosyltransferase)
-4.40	Hs.79340 PTH-responsive osteosarcoma B1 protein
-4.36	Hs.198037 KIAA0599 protein
-4.22	Hs.104555 neuropeptide FF-amide peptide precursor
-4.21	Hs.76930 synuclein, alpha (non A4 component of amyloid precursor)
-4.21	Hs.286124 CD24 antigen (small cell lung carcinoma cluster 4 antigen)
-4.07	Hs.234642 aquaporin 3
-3.88	Hs.89535 bactericidalpermeability-increasing protein
-3.88	Hs.88411 lymphocyte antigen 117
-3.84	Hs.58362 hypothetical protein FLJ12681
-3.81	Hs.154567 supervillin
-3.72	Hs.73839 ribonuclease, RNase A family, 3 (eosinophil cationic protein)
-3.72	Hs.272108 ESTs
-3.69	CD24 antigen (small cell lung carcinoma cluster 4 antigen)
-3.65	Hs.75498 small inducible cytokine subfamily A (Cys-Cys), member 20
-3.65	Hs.159454 ESTs
-3.63	Hs.76289 biliverdin reductase B (flavin reductase (NADPH))
-3.33	Hs.150917 catenin (cadherin-associated protein), alpha 2
-3.30	Hs.296941 H factor (complement)-like 2
-3.20	Hs.26994 hypothetical protein FLJ20477
-3.19	Hs.318885 superoxide dismutase 2, mitochondrial
-3.18	Hs.18889 DKFZP434M183 protein
-3.10	Hs.2962 S100 calcium-binding protein P
-3.05	Hs.181353 UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2
-3.03	Hs.286124 CD24 antigen (small cell lung carcinoma cluster 4 antigen)
-2.97	Hs.80741 propionyl Coenzyme A carboxylase, alpha polypeptide
-2.96	Hs.572 orosomucoid 1
-2.96	Hs.332045 Homo sapiens cDNA FLJ20161 fis, clone COL09252, highly similar to L33930 Homo sapiens CD24 signal transducer
-2.91	Hs.251754 secretory leukocyte protease inhibitor (antileukoproteinase)
-2.87	Hs.30898 KIAA0634 protein
-2.84	Hs.2582 defensin, alpha 4, corticostatin
-2.76	Hs.1174 cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4)
-2.76	Hs.8109 hypothetical protein FLJ21080
-2.73	Hs.7258 hypothetical protein FLJ22021
-2.71	aquaporin 3
-2.68	Hs.153934 core-binding factor, runt domain, alpha subunit 2; translocated to, 2
-2.66	Hs.193716 complement component (3b4b) receptor 1, including Knops blood group system

FIGURE 3

Table 1
Differential Gene Expression in Chemokinesis vs Medium SDF-1 Gradients

-2.59	Hs.814 major histocompatibility complex, class II, DP beta 1
-2.59	Hs.1619 achaete-scute complex (Drosophila) homolog-like 1
-2.58	Hs.100602 MAD (mothers against decapentaplegic, Drosophila) homolog 7
-2.56	Hs.189109 hypothetical protein FLJ21458
-2.55	Hs.328822 haptoglobin-related protein
-2.55	Hs.17752 phosphatidylserine-specific phospholipase A1alpha
-2.54	Hs.100623 phospholipase C, beta 3, neighbor pseudogene
-2.53	Hs.103382 phospholipid scramblase 3
-2.50	Hs.193122 Fc fragment of IgA, receptor for
-2.49	Hs.153952 5 nucleotidase (CD73)
-2.49	Hs.322422 Homo sapiens cDNA FLJ11676 fis, clone HEMBA1004752, highly similar to Homo sapiens mRNA for LAK-4p
-2.48	Hs.204238 lipocalin 2 (oncogene 24p3)
-2.45	gb:AF251061.1 /DEF=Homo sapiens neurocalcin mRNA, complete cds.
-2.45	Hs.192662 hypothetical protein FLJ10469
-2.44	Hs.241053 ESTs
-2.43	Hs.288300 hypothetical protein FLJ23231
-2.42	Hs.323664 nudix (nucleoside diphosphate linked moiety X)-type motif 6
-2.41	Hs.7531 KIAA0810 protein
-2.40	Hs.7252 KIAA1224 protein
-2.40	Hs.12229 TGFB inducible early growth response 2
-2.37	Hs.72964 makorin, ring finger protein, 3
-2.36	Hs.272205 hypothetical protein FLJ10034
-2.34	Hs.10082 potassium intermediatesmall conductance calcium-activated channel, subfamily N, member 4
-2.32	Hs.300711 annexin A5
-2.32	Hs.914 Human mRNA for SB classII histocompatibility antigen alpha-chain
-2.31	Hs.278503 regulated in glioma
-2.30	Hs.75703 small inducible cytokine A4 (homologous to mouse Mip-1b)
-2.26	Hs.75811 N-acylsphingosine amidohydrolase (acid ceramidase)
-2.25	Hs.81256 S100 calcium-binding protein A4 (calcium protein, calvasculin, metastasin, murine placental homolog)
-2.25	Hs.3066 granzyme K (serine protease, granzyme 3; tryptase II)
-2.24	Hs.71746 hypothetical protein FLJ11583
-2.23	Hs.155191 villin 2 (ezrin)
-2.23	Hs.159263 collagen, type VI, alpha 2
-2.23	Hs.21497 Homo sapiens, clone IMAGE:3629896, mRNA, partial cds
-2.22	Hs.9973 tensin
-2.20	Hs.119274 RAS p21 protein activator (GTPase activating protein) 3 (Ins(1,3,4,5)P4-binding protein)
-2.18	Hs.15984 pp21 homolog
-2.16	Hs.99491 RAS guanyl releasing protein 2 (calcium and DAG-regulated)
-2.16	Hs.17409 cysteine-rich protein 1 (intestinal)
-2.15	Hs.76297 G protein-coupled receptor kinase 6
-2.15	Hs.152981 CDP-diacylglycerol synthase (phosphatidate cytidylyltransferase) 1
-2.14	Hs.957 putative opioid receptor, neuromedin K (neurokinin B) receptor-like
-2.14	Hs.168132 interleukin 15
-2.10	Hs.79021 tafazzin (cardiomyopathy, dilated 3A (X-linked); endocardial fibroelastosis 2; Barth syndrome)
-2.07	Hs.31659 thyroid hormone receptor-associated protein, 95-kD subunit
-2.05	Hs.167017 gamma-aminobutyric acid (GABA) B receptor, 1
-2.05	Hs.301289 Homo sapiens cDNA FLJ12427 fis, clone MAMMA1003127, highly similar to MYOSIN I ALPHA
-2.02	Hs.103147 hypothetical protein FLJ21347
-2.02	Hs.7188 hypothetical protein FLJ20369
-2.01	Hs.29656 cyclin-dependent kinase inhibitor 2D (p19, inhibits CDK4)
-2.01	Hs.303289 Homo sapiens cDNA FLJ14096 fis, clone MAMMA1000752
-2.01	Hs.293699 hypothetical protein FLJ20495

FIGURE 3

Table 1
Differential Gene Expression in Chemokinesis vs Medium SDF-1 Gradients

-2.00	Hs.234799 breakpoint cluster region
-1.99	Hs.50868 solute carrier family 22 (organic cation transporter), member 1-like
-1.99	Hs.182982 golgin-67
-1.98	Hs.195464 filamin A, alpha (actin-binding protein-280)
-1.96	Hs.198252 G protein-coupled receptor 9
-1.96	Hs.56186 EGF-like-domain, multiple 3
-1.95	Hs.74034 Homo sapiens clone 24651 mRNA sequence
-1.95	Hs.11809 single Ig IL-1R-related molecule
-1.94	Hs.2551 adrenergic, beta-2-, receptor, surface
-1.93	Hs.154299 coagulation factor II (thrombin) receptor-like 1
-1.93	Hs.195464 filamin A, alpha (actin-binding protein-280)
-1.90	Hs.100071 6-phosphogluconolactonase
-1.89	Hs.79601 /len=613
-1.89	Hs.195464 filamin A, alpha (actin-binding protein-280)
-1.88	Hs.11809 /len=525
-1.87	Hs.94382 adenosine kinase
-1.87	Hs.134514 ATP-binding cassette, sub-family A (ABC1), member 7
-1.85	Hs.64310 interleukin 11 receptor, alpha
-1.83	Hs.78909 butyrate response factor 2 (EGF-response factor 2)
-1.81	PTH-responsive osteosarcoma B1 protein
-1.81	Hs.31290 Homo sapiens clone 23832 mRNA sequence
-1.81	Hs.30783 hypothetical protein FLJ20850
-1.81	Hs.9196 hypothetical protein
-1.80	Hs.332173 transducin-like enhancer of split 2, homolog of Drosophila E(sp1)
-1.79	Hs.4764 KIAA0763 gene product
-1.79	Hs.14770 bridging integrator 2
-1.79	Hs.178011 hypothetical protein FLJ20257
-1.79	Hs.13405 gephyrin
-1.78	gb:M18728.1 /DEF=Human nonspecific crossreacting antigen mRNA, complete cds.
-1.77	Hs.76240 adenylate kinase 1
-1.75	Hs.79404 neuron-specific protein
-1.74	Hs.106061 RD RNA-binding protein
-1.74	Hs.8297 ribonuclease 6 precursor
-1.73	Hs.115907 diacylglycerol kinase, delta (130kD)
-1.73	Hs.40300 calpain 3, (p94)
-1.73	Hs.16193 Homo sapiens mRNA; cDNA DKFZp586B211 (from clone DKFZp586B211)
-1.73	Hs.321197 PDZ domain protein (Drosophila inaD-like)
-1.73	Hs.7212 hypothetical protein PP1044
-1.73	Hs.181780 hypothetical protein FLJ20241
-1.72	Hs.182982 golgin-67
-1.72	Hs.132807 Homo sapiens (clone 3.8-1) MHC class I mRNA fragment
-1.71	Hs.193163 bridging integrator 1
-1.71	Hs.115460 calicin
-1.71	Hs.193163 bridging integrator 1
-1.70	Hs.75450 delta sleep inducing peptide, immunoreactor
-1.70	Hs.1432 protein kinase C substrate 80K-H
-1.70	Hs.6150 Rho-specific guanine nucleotide exchange factor p114

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

UP REGULATED IN FUGETAXIS COMPARED TO CHEMOTAXIS SDF-1 GRADIENTS

11.00	Hs.75184 chitinase 3-like 1 (cartilage glycoprotein-39)
8.12	Hs.79658 casein kinase 1, epsilon
6.17	Hs.7358 hypothetical protein FLJ13110
5.66	Hs.89535 bactericidalpermeability-increasing protein
5.61	Hs.100000 S100 calcium-binding protein A8 (calgranulin A)
5.57	Hs.182740 ribosomal protein S11
5.15	Hs.78913 chemokine (C-X3-C) receptor 1
5.07	Hs.81665 v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog
5.02	Hs.247989 Human immunoglobulin heavy chain variable region (V4-30.2) gene, partial cds
4.93	Hs.146409 cell division cycle 42 (GTP-binding protein, 25kD)
4.71	Hs.3076 MHC class II transactivator
4.70	gb:AF262973.1 /DEF=Homo sapiens killer cell immunoglobulin-like receptor 3DL1 (KIR3DL1) mRNA, KIR3DL1*00701 allele, complete cds.
4.57	gb:NM_000961.1 /DEF=Homo sapiens prostaglandin I2 (prostacyclin) synthase (PTGIS), mRNA.
4.44	Hs.2962 S100 calcium-binding protein P
4.37	Hs.127384 DKFZP564C196 protein
4.34	Hs.108502 hypothetical protein FLJ20150
4.33	Hs.56328 killer cell immunoglobulin-like receptor, three domains, long cytoplasmic tail, 2
4.28	Hs.75137 KIAA0193 gene product
4.21	Hs.57975 calsequestrin 2 (cardiac muscle)
4.12	Hs.44579 hypothetical protein FLJ20199
4.08	Hs.326737 Homo sapiens, clone MGC:4655, mRNA, complete cds
3.99	Hs.13040 G protein-coupled receptor 86
3.98	Hs.75106 clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)
3.96	Hs.75990 haptoglobin
3.91	Hs.6164 hypothetical protein FLJ10698
3.86	Hs.193783 Human DNA sequence from clone RP13-329D4 on chromosome 20 Contains ESTs, STSs, GSSs and a CpG island. Contains the 3 part of a novel gene, a gene similar to NCOR1 for a truncated form of nuclear receptor co-repressor 1 (retinoid X receptor inte
3.80	Hs.274272 hypothetical protein FLJ10232
3.78	Hs.111867 GLI-Kruppel family member GLI2
3.72	Hs.75105 emopamil-binding protein (sterol isomerase)
3.71	Hs.116651 epithelial V-like antigen 1
3.65	Hs.223014 antizyme inhibitor
3.64	Hs.180884 carboxypeptidase B1 (tissue)
3.64	Hs.314762 Homo sapiens partial IGKV gene for immunoglobulin kappa chain variable region, clone 30
3.62	Hs.80620 guanine nucleotide exchange factor for Rap1; M-Ras-regulated GEF
3.58	Hs.44278 hypothetical protein FLJ12538 similar to ras-related protein RAB17
3.57	Hs.29417 HCF-binding transcription factor Zhangfei
3.56	Hs.105859 hypothetical protein FLJ10260
3.55	Hs.154495 acetylcholinesterase (YT blood group)
3.54	Hs.287269 chorionic somatomammotropin hormone-like 1
3.51	Hs.2582 defensin, alpha 4, corticostatin
3.45	Hs.98658 budding uninhibited by benzimidazoles 1 (yeast homolog)
3.42	Hs.226014 Human DNA sequence from clone 240B8 on chromosome 6p11.2-q12. Contains the 3 part of a gene for a novel protein similar to T-STAR, Etoile, Sam68, SLM1 and p62 Tyrosine Phosphoprotein. Contains ESTs, STSs, GSSs and genomic marker D6S1695
3.42	Hs.33102 transcription factor AP-2 beta (activating enhancer-binding protein 2 beta)
3.34	Hs.18894 /len=982
3.29	Hs.287539 hypothetical protein FLJ12662
3.28	Hs.114316 sialyltransferase 8C (alpha2,3Galbeta1,4GlcNAcalpha 2,8-sialyltransferase)
3.27	Hs.323511 Homo sapiens cDNA: FLJ23176 fis, clone LNG10452
3.24	Hs.89839 EphA1
3.23	Hs.298469 angiotensin I converting enzyme (peptidyl-dipeptidase A) 1
3.18	Hs.314452 fibrousheathin II
3.17	Hs.85181 v-raf-1 murine leukemia viral oncogene homolog 1
3.16	Hs.273621 Homo sapiens cDNA: FLJ21350 fis, clone COL02751

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

3.11	Hs.88411 lymphocyte antigen 117
3.10	Hs.2056 UDP glycosyltransferase 1 family, polypeptide A9
3.10	Hs.233634 hypothetical protein FLJ14220
3.09	Hs.284277 Homo sapiens immunoglobulin mu chain antibody MO30 (IgM) mRNA, complete cds
3.09	gb:BC006196.1 /DEF=Homo sapiens, tumor necrosis factor receptor superfamily, member 9, clone MGC:2172, mRNA, complete cds.
3.07	Hs.97084 lymphocyte antigen 94 (mouse) homolog (activating NK-receptor ; NK-p46)
3.05	Hs.172740 microtubule-associated protein, RPEB family, member 3
3.00	Hs.73838 Homo sapiens (clone Z146) retinal mRNA, 3 end and repeat region
2.99	Hs.75294 corticotropin releasing hormone
2.99	Hs.949 neutrophil cytosolic factor 2 (65kD, chronic granulomatous disease, autosomal 2)
2.99	Hs.278984 calcium binding protein 2
2.99	Hs.73793 vascular endothelial growth factor
2.97	Hs.37169 potassium inwardly-rectifying channel, subfamily J, member 3
2.97	gb:NM_030876.1 /DEF=Homo sapiens olfactory receptor, family 5, subfamily V member 1 (OR5V1), mRNA.
2.96	Hs.88411 lymphocyte antigen 117
2.96	Hs.38586 hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1
2.95	Hs.65746 KIAA0318 protein
2.95	Hs.74076 CD163 antigen
2.91	Hs.40434 ribosomal protein S6 kinase, 90kD, polypeptide 6
2.90	Hs.137569 tumor protein 63 kDa with strong homology to p53
2.89	Hs.128749 alpha-methylacyl-CoA racemase
2.88	Hs.93758 H4 histone family, member H
2.84	Hs.7936 BAI1-associated protein 2
2.84	Hs.15165 novel retinal pigment epithelial gene
2.82	Hs.16488 calreticulin
2.81	Hs.79706 plectin 1, intermediate filament binding protein, 500kD
2.81	Hs.98485 gap junction protein, beta 3, 31kD (connexin 31)
2.80	Hs.246107 elongation of very long chain fatty acids (FEN1Elo2, SUR4Elo3, yeast)-like 2
2.80	Hs.287644 hypothetical protein FLJ20972
2.76	Hs.10755 dihydropyrimidinase
2.76	Hs.4 alcohol dehydrogenase 2 (class I), beta polypeptide
2.75	Hs.73839 ribonuclease, RNase A family, 3 (eosinophil cationic protein)
2.75	Hs.199250 chloride channel 4
2.73	Hs.198427 hexokinase 2
2.72	Hs.274127 CLST 11240 protein
2.71	Hs.70823 KIAA1077 protein
2.69	Hs.75260 mitogen inducible 2
2.68	Hs.302022 PR domain containing 16
2.67	Hs.621 lectin, galactoside-binding, soluble, 3 (galectin 3)
2.65	Hs.287872 hypothetical protein FLJ14106
2.65	Hs.123062 Human mRNA for T cell receptor, clone IGRA24
2.62	Hs.83484 SRY (sex determining region Y)-box 4
2.62	Hs.307138 Human DNA sequence from clone RP3-508D13 on chromosome 6 Contains a heat shock protein DNAJ pseudogene, ESTs, STSs and GSSs
2.62	Hs.151449 KIAA0535 gene product
2.60	Hs.1310 CD1B antigen, b polypeptide
2.59	Hs.6580 Homo sapiens cDNA: FLJ23227 fis, clone CAE00645, highly similar to AF052138 Homo sapiens clone 23718 mRNA sequence
2.59	gb:NM_030788.1 /DEF=Homo sapiens DC-specific transmembrane protein (LOC81501), mRNA.
2.59	Hs.132942 GTPase regulator associated with the focal adhesion kinase pp125(FAK); KIAA0621 protein
2.58	Hs.169401 apolipoprotein E
2.56	Hs.19520 FXYD domain-containing ion transport regulator 2
2.56	Hs.97403 KIAA0944 protein
2.52	Hs.181307 H3 histone, family 3A
2.51	Hs.119140 eukaryotic translation initiation factor 5A
2.49	Hs.307104 Human DNA sequence from clone RP11-278J20 on chromosome 6. Contains ESTs, STSs and GSSs. Contains an RBBP4 (retinoblastoma-binding protein 4) pseudogene and a KIAA0797 pseudogene
2.46	Hs.301916 Homo sapiens microtubule-associated protein 1A like protein (M1LP) mRNA, partial cds

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

2.45	Hs.79564 neuronal PAS domain protein 1
2.44	Hs.285529 G protein-coupled receptor 49
2.43	Hs.275215 hydroxysteroid (11-beta) dehydrogenase 1
2.41	Hs.128311 ESTs
2.40	Hs.37142 ephrin-A5
2.38	Hs.177972 chromosome 4 open reading frame 6
2.38	Hs.79516 brain abundant, membrane attached signal protein 1
2.36	Hs.152292 SWISNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 1
2.36	Hs.97984 hypothetical protein FLJ22252 similar to SRY-box containing gene 17
2.35	gb:AB059408.1 /DEF=Homo sapiens mRNA, complete cds, clone:SMAP31-12.
2.34	Hs.88411 lymphocyte antigen 117
2.33	Hs.113274 transcription factor EC
2.32	Hs.166715 hypothetical protein PRO2533
2.29	Hs.73739 5-hydroxytryptamine (serotonin) receptor 7 (adenylate cyclase-coupled)
2.29	Hs.2718 human epididymis-specific 3 alpha
2.28	Hs.158316 ATP-binding cassette, sub-family B (MDRTAP), member 11
2.27	Hs.2012 transcobalamin I (vitamin B12 binding protein, R binder family)
2.26	Hs.301959 proline synthetase co-transcribed (bacterial homolog)
2.21	Hs.172153 glutathione peroxidase 3 (plasma)
2.20	Hs.183805 ankyrin 1, erythrocytic
2.18	Hs.284136 PRO2047 protein
2.18	Hs.181341 Homo sapiens cDNA FLJ14307 fis, clone PLACE3000158
2.17	Hs.232447 Homo sapiens DNA sequence from PAC 127D3 on chromosome 1q23-25. Contains FMO2 and FMO3 genes for Flavin-containing Monooxygenase 2 and Flavin-containing Monooxygenase 3 (Dimethylaniline Monooxygenase (N-Oxide 3, EC1.14.13.8, Dimethylaniline Oxi
2.16	Hs.77202 protein kinase C, beta 1
2.16	Hs.287673 hypothetical protein FLJ21625
2.16	Hs.76666 C9orf10 protein
2.16	Hs.150443 KIAA0320 protein
2.15	Hs.301946 lymphoid blast crisis oncogene
2.14	Hs.287427 Homo sapiens cDNA FLJ11578 fis, clone HEMBA1003571
2.13	Hs.107526 UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 5
2.12	Hs.54481 low density lipoprotein receptor-related protein 8, apolipoprotein e receptor
2.12	Hs.268531 granzyme M (lymphocyte met-ase 1)
2.10	Hs.77886 lamin AC
2.10	Hs.176090 PRKC, apoptosis, WT1, regulator
2.10	Hs.306752 Homo sapiens cDNA: FLJ21391 fis, clone COL03479
2.10	Hs.210859 hypothetical protein FLJ11016
2.09	Hs.127614 protein phosphatase 1, regulatory (inhibitor) subunit 3 (glycogen and sarcoplasmic reticulum binding subunit, skeletal muscle)
2.08	Hs.82422 capping protein (actin filament), gelsolin-like
2.08	Hs.32168 KIAA0442 protein
2.08	Hs.78305 RAB2, member RAS oncogene family
2.07	Hs.306667 Homo sapiens cDNA FLJ14076 fis, clone HEMBB1001925
2.07	Hs.326198 transcription factor 4
2.06	Hs.60708 calsequestrin 1 (fast-twitch, skeletal muscle)
2.06	Hs.1870 phenylalanine hydroxylase
2.05	Hs.217493 annexin A2
2.05	Hs.33084 solute carrier family 2 (facilitated glucose transporter), member 5
2.05	Hs.80758 aspartyl-tRNA synthetase
2.04	Hs.73291 hypothetical protein FLJ10881
2.03	Hs.270549 HZFw1 protein
2.00	Hs.5831 tissue inhibitor of metalloproteinase 1 (erythroid potentiating activity, collagenase inhibitor)
2.00	Hs.142023 T cell activation, increased late expression
2.00	Hs.272789 hypothetical protein FLJ20217
2.00	Hs.306711 Homo sapiens cDNA: FLJ21215 fis, clone COL00526
2.00	Hs.323409 Homo sapiens cDNA FLJ14113 fis, clone MAMMA1001715
1.99	Hs.41143 phosphoinositide-specific phospholipase C-beta 1
1.99	Hs.46752 nitric oxide synthase 1 (neuronal)

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

1.98	Hs.278950 protocadherin beta 1
1.97	Hs.13245 KIAA0455 gene product
1.97	Hs.14070 hypothetical protein FLJ14166
1.96	Hs.269926 Homo sapiens cDNA: FLJ21441 fis, clone COL04422
1.96	Hs.26776 neurotrophic tyrosine kinase, receptor, type 3
1.96	Hs.159003 transient receptor potential channel 6
1.96	Hs.74614 tight junction protein 1 (zona occludens 1)
1.95	Hs.272351 Human DNA sequence from clone RP4-746H2 on chromosome 20. Contains a pseudogene similar to prokaryotic RPS11 (30S ribosomal protein S11), ESTs, STSs and GSSs
1.94	Hs.5814 suppression of tumorigenicity 7
1.94	Hs.169824 killer cell lectin-like receptor subfamily B, member 1
1.94	Hs.283683 chromosome 8 open reading frame 4
1.94	Hs.326780 Homo sapiens clone KM35 immunoglobulin light chain variable region mRNA, partial cds
1.94	Hs.106185 ral guanine nucleotide dissociation stimulator
1.93	Hs.172471 potassium voltage-gated channel, shaker-related subfamily, beta member 1
1.93	Hs.6654 KIAA0657 protein
1.92	Hs.158343 Testis-specific PTP-BL-related protein on Y
1.92	Hs.35101 proline-rich Gla (G-carboxyglutamic acid) polypeptide 2
1.92	Hs.97109 ESTs
1.92	Hs.106552 cell recognition molecule Caspr2
1.91	Hs.153445 Human mRNA for unknown product, partial cds
1.91	Hs.12079 calsyntenin-2
1.91	Hs.69547 myelin basic protein
1.90	Hs.129914 runt-related transcription factor 1 (acute myeloid leukemia 1; aml1 oncogene)
1.90	Hs.143212 cystatin F (leukocystatin)
1.90	Hs.90291 laminin, beta 2 (laminin S)
1.89	Hs.287719 hypothetical protein FLJ23074
1.88	Hs.91448 MKP-1 like protein tyrosine phosphatase
1.88	Hs.21858 trinucleotide repeat containing 3
1.88	Hs.77436 pleckstrin
1.88	Hs.295112 KIAA0618 gene product
1.87	Hs.76136 thioredoxin
1.87	Hs.247877 Human DNA sequence from clone 263J7 on chromosome 6q14.3-15. Contains an RPL7 (60S Ribosomal Protein L7) pseudogene, a RAB1 (RAB1, member RAS oncogene family) pseudogene, ESTs, an STS and GSSs
1.87	Hs.7358 hypothetical protein FLJ13110
1.86	Hs.128322 t-complex 11 (a murine tcp homolog)
1.86	Hs.226019 Homo sapiens mRNA for G16 protein (G16 gene located in the class III region of the major histocompatibility complex)
1.86	Hs.183805 ankyrin 1, erythrocytic
1.86	Hs.326401 fibroblast growth factor 12B
1.85	Hs.73729 very low density lipoprotein receptor
1.85	Hs.211578 MAD (mothers against decapentaplegic, Drosophila) homolog 3
1.85	Hs.158344 testis-specific testis transcript Y 1
1.84	Hs.114765 myeloidlymphoid or mixed-lineage leukemia (trithorax (Drosophila) homolog); translocated to, 2
1.84	Hs.123136 leucine rich repeat and death domain containing protein
1.84	Hs.307185 Human glycophorin HeP2 mRNA, partial cds
1.84	Hs.81892 KIAA0101 gene product
1.83	Hs.160483 erythrocyte membrane protein band 7.2 (stomatin)
1.83	Hs.82962 thymidylate synthetase
1.83	Hs.119285 /len=716
1.82	Hs.149255 phosphatidylinositol-4-phosphate 5-kinase, type I, alpha
1.82	Hs.169910 KIAA0173 gene product
1.82	Hs.75825 pleiomorphic adenoma gene-like 1
1.82	Hs.89474 ADP-ribosylation factor 6
1.81	Hs.272398 transcription factor ets
1.81	Hs.296756 Homo sapiens cDNA FLJ14348 fis, clone THYRO1001602
1.81	Hs.274578 Homo sapiens mRNA; cDNA DKFZp434F0723 (from clone DKFZp434F0723)
1.80	Hs.198281 pyruvate kinase, muscle

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

1.80	Hs.158345 testis-specific testis transcript Y 2
1.80	Hs.180919 inhibitor of DNA binding 2, dominant negative helix-loop-helix protein
1.80	Hs.10247 activated leucocyte cell adhesion molecule
1.80	Hs.132781 class I cytokine receptor
1.80	Hs.54481 low density lipoprotein receptor-related protein 8, apolipoprotein e receptor
1.79	Hs.48778 niban protein
1.79	Hs.9329 chromosome 20 open reading frame 1
1.79	Hs.272798 hypothetical protein FLJ20413
1.79	Hs.100194 arachidonate 5-lipoxygenase-activating protein
1.78	Hs.270010 KIAA0508 protein
1.78	Hs.6088 a disintegrin and metalloproteinase domain 11
1.78	Hs.183075 ATPase, Ca++ transporting, cardiac muscle, fast twitch 1
1.78	Hs.272375 WNT16 protein
1.78	Hs.288983 hypothetical protein FLJ21477
1.78	Hs.92254 hypothetical protein FLJ20163
1.78	Hs.306531 Homo sapiens caspase-10c mRNA, complete cds
1.78	Hs.76722 CCAATenhancer binding protein (CEBP), delta
1.77	Hs.76901 for protein disulfide isomerase-related
1.77	Hs.254105 enolase 1, (alpha)
1.77	Hs.311 phosphoribosyl pyrophosphate amidotransferase
1.77	Hs.31869 /len=680
1.77	Hs.30299 IGF-II mRNA-binding protein 2
1.77	Hs.18705 KIAA1233 protein
1.77	Hs.121084 eppin-3
1.76	intersectin 1 (SH3 domain protein)
1.76	Hs.169081 ets variant gene 6 (TEL oncogene)
1.76	Hs.4975 potassium voltage-gated channel, KQT-like subfamily, member 2
1.76	Hs.170076 variable charge, Y chromosome
1.75	Hs.135305 olfactory receptor, family 10, subfamily H, member 3
1.75	Hs.287388 histamine H4 receptor
1.75	Hs.165 glucagon-like peptide 1 receptor
1.74	Hs.306235 hypothetical protein FLJ13954
1.73	Hs.102865 interleukin 1 receptor-like 2
1.73	Hs.49500 KIAA0746 protein
1.73	Hs.56175 H.sapiens gene from PAC 106H8, similar to Dynamin
1.73	Hs.224829 ESTs
1.73	Hs.287445 hypothetical protein FLJ11726
1.72	Hs.287608 hypothetical protein FLJ13892
1.72	Hs.3628 mitogen-activated protein kinase kinase kinase kinase 4
1.72	Hs.97174 potassium inwardly-rectifying channel, subfamily K, member 4
1.72	Hs.283330 hypothetical protein PRO1843
1.72	Hs.274509 T cell receptor gamma constant 2
1.71	Hs.105115 absent in melanoma 2
1.71	Hs.121576 Homo sapiens cDNA FLJ20153 fis, clone COL08656, highly similar to AJ001381 Homo sapiens incomplete cDNA for a mutated allele
1.71	Hs.183556 solute carrier family 1 (neutral amino acid transporter), member 5
1.71	Hs.79732 fibulin 1
1.71	Hs.62954 ferritin, heavy polypeptide 1
1.70	Hs.88474 prostaglandin-endoperoxide synthase 1 (prostaglandin GH synthase and cyclooxygenase)
1.70	Hs.112259 T cell receptor gamma locus
1.70	Hs.11 carcinoembryonic antigen-related cell adhesion molecule 3

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

UP REGULATED IN CHEMOTAXIS COMPARED TO FUGETAXIS SDF-1 GRADIENTS	
-21.01	Hs.323342 actin related protein 23 complex, subunit 4 (20 kD)
-14.05	Hs.78409 collagen, type XVIII, alpha 1
-10.49	Hs.15075 hypothetical protein DKFZp434E2216
-10.32	Hs.305960 hemoglobin, gamma A
-10.19	Hs.85752 uncharacterized hematopoietic stemprogenitor cells protein MDS026
-9.17	Hs.76415 inter-alpha (globulin) inhibitor H4 (plasma Kallikrein-sensitive glycoprotein)
-8.59	Hs.740 PTK2 protein tyrosine kinase 2
-7.79	Hs.29222 zinc finger protein 76 (expressed in testis)
-7.50	Hs.73931 major histocompatibility complex, class II, DQ beta 1
-7.30	Hs.82979 mitogen-activating protein kinase kinase kinase kinase 2
-6.96	Hs.46907 HEMK homolog 7kb
-6.76	Hs.289031 hypothetical protein FLJ11848
-6.59	Hs.79410 solute carrier family 4, anion exchanger, member 2 (erythrocyte membrane protein band 3-like 1)
-6.29	Hs.109441 hypothetical protein FLJ20707
-6.02	Hs.14142 nudix (nucleoside diphosphate linked moiety X)-type motif 2
-5.92	Hs.110457 Wolf-Hirschhorn syndrome candidate 1
-5.76	Hs.247981 Stat2 type a
-5.62	Hs.301636 peroxisomal biogenesis factor 6
-5.43	Hs.283404 organic cation transporter
-5.30	Hs.300496 mitochondrial solute carrier
-5.28	Hs.79019 baculoviral IAP repeat-containing 1
-5.28	Hs.6343 KIAA1464 protein
-5.27	Hs.121073 hypothetical protein FLJ10466
-5.25	Hs.280666 Homo sapiens chromosome 19, cosmid R32184
-5.25	Hs.79340 PTH-responsive osteosarcoma B1 protein
-5.12	Hs.279862 cdk inhibitor p21 binding protein
-5.07	gb:NM_030882.1 /DEF=Homo sapiens apolipoprotein L, 2 (APOL2), mRNA.
-4.97	Hs.76289 biliverdin reductase B (flavin reductase (NADPH))
-4.96	Hs.36972 CD7 antigen (p41)
-4.95	Hs.21970 guanine nucleotide binding protein (G protein), gamma 3, linked
-4.82	Hs.197335 plasma glutamate carboxypeptidase
-4.73	Hs.5378 spondin 1, (f-spondin) extracellular matrix protein
-4.67	Hs.250821 hypothetical protein MGC4054
-4.65	Hs.93597 cyclin-dependent kinase 5, regulatory subunit 1 (p35)
-4.63	Hs.22370 Homo sapiens mRNA; cDNA DKFZp564O0122 (from clone DKFZp564O0122)
-4.51	Hs.1516 insulin-like growth factor-binding protein 4
-4.49	Hs.74047 electron-transfer-flavoprotein, beta polypeptide
-4.48	Hs.22479 KIAA1110 protein
-4.46	Hs.296821 Human facioscapulohumeral muscular dystrophy (FSHD) gene region, D4Z4 tandem repeat unit
-4.46	Hs.20017 chromosome 22 open reading frame 4
-4.45	Hs.325530 KIAA1067 protein
-4.44	Hs.26938 Homo sapiens, clone IMAGE:4053044, mRNA, partial cds
-4.37	Hs.23585 KIAA1078 protein
-4.36	Hs.264 GS2 gene
-4.32	Hs.99987 excision repair cross-complementing rodent repair deficiency, complementation group 2 (xeroderma pigmentosum D)
-4.30	Hs.7943 RPB5-mediating protein
-4.26	Hs.27610 retinoic acid- and interferon-inducible protein (58kD)
-4.24	Hs.278483 H4 histone family, member E
-4.20	Hs.26045 protein tyrosine phosphatase, receptor type, A
-4.16	Hs.155924 cAMP responsive element modulator
-4.13	Hs.54558 hypothetical protein FLJ22222
-4.04	Hs.7946 KIAA1288 protein
-4.04	Hs.29285 ZYG homolog
-4.01	Hs.112751 KIAA0892 protein
-3.96	Hs.7019 signal-induced proliferation-associated gene 1

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

-3.95	Hs.80598 transcription elongation factor A (SII), 2
-3.93	Hs.315478 Homo sapiens, Similar to pericentriolar material 1, clone MGC:8458, mRNA, complete cds
-3.93	Hs.272814 hypothetical protein DKFZp434E1723
-3.92	Hs.277401 bromodomain adjacent to zinc finger domain, 2A
-3.92	Hs.287652 Homo sapiens cDNA: FLJ21258 fis, clone COL01408
-3.88	Hs.41693 DnaJ (Hsp40) homolog, subfamily B, member 4
-3.86	Hs.19554 chromosome 1 open reading frame 2
-3.84	Hs.112434 Novel human gene mapping to chomosome 13
-3.80	Hs.4854 cyclin-dependent kinase inhibitor 2C (p18, inhibits CDK4)
-3.77	Hs.182577 inositol polyphosphate-5-phosphatase, 75kD
-3.77	Hs.181223 hypothetical protein PRO2801
-3.77	Hs.256549 nucleotide binding protein 2 (E.coli MinD like)
-3.73	gb:U41742.1 /DEF=Human nucleophosmin-retinoic acid receptor alpha fusion protein NPM-RAR long form mRNA, complete cds.
-3.65	thyroid hormone receptor, alpha (avian erythroblastic leukemia viral (v-erb-a) oncogene homolog)
-3.64	Hs.30250 v-maf musculoaponeurotic fibrosarcoma (avian) oncogene homolog
-3.64	Hs.44865 lymphoid enhancer binding factor-1
-3.63	Hs.40300 calpain 3, (p94)
-3.63	gb:Z25432.1 /DEF=H.sapiens protein-serinethreonine kinase gene, complete CDS.
-3.62	Hs.90443 NADH dehydrogenase (ubiquinone) Fe-S protein 8 (23kD) (NADH-coenzyme Q reductase)
-3.62	Hs.121102 vanin 2
-3.61	Hs.126707 hypothetical protein FLJ11457
-3.61	Hs.306677 Homo sapiens cDNA FLJ14320 fis, clone PLACE3000455
-3.61	Hs.33862 ESTs
-3.59	Hs.139648 KIAA0706 gene product
-3.59	Hs.89560 iduronidase, alpha-L-
-3.57	Hs.7426 KIAA0841 protein
-3.56	Hs.5378 spondin 1, (f-spondin) extracellular matrix protein
-3.56	Hs.14286 flavin containing monooxygenase 5
-3.56	Hs.319088 hypothetical protein FLJ10375
-3.55	Hs.138155 carbohydrate (N-acetylglucosamine 6-O) sulfotransferase 7
-3.55	Hs.129943 KIAA0545 protein
-3.53	Hs.89232 chromobox homolog 5 (Drosophila HP1 alpha)
-3.50	Hs.142245 HERV-H LTR-associating 3
-3.49	Hs.26899 KIAA0285 gene product
-3.49	Hs.77313 cyclin-dependent kinase (CDC2-like) 10
-3.47	Hs.78146 plateletendothelial cell adhesion molecule (CD31 antigen)
-3.47	Hs.194148 v-yes-1 Yamaguchi sarcoma viral oncogene homolog 1
-3.44	Hs.21361 KIAA1023 protein
-3.43	Hs.227280 U6 snRNA-associated Sm-like protein
-3.42	Hs.9846 KIAA1040 protein
-3.41	Hs.73742 ribosomal protein, large, P0
-3.40	Hs.226581 COX15 (yeast) homolog, cytochrome c oxidase assembly protein
-3.35	Hs.1975 hypothetical protein FLJ21007
-3.33	Hs.100090 tetraspan 3
-3.29	Hs.195484 Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 327506
-3.29	Hs.85195 myeloid leukemia factor 1
-3.27	Hs.155470 zinc finger protein 38 (KOX 25)
-3.27	Hs.6831 golgi resident protein GCP60
-3.25	Hs.87908 Snf2-related CBP activator protein
-3.23	Hs.12908 CDC42-binding protein kinase beta (DMPK-like)
-3.22	Hs.210546 interleukin 21 receptor
-3.20	Hs.46821 hypothetical protein FLJ20086
-3.16	Hs.211933 collagen, type XIII, alpha 1
-3.16	Hs.36977 hemoglobin, delta
-3.15	Hs.291972 ESTs, Moderately similar to SC14_HUMAN SEC14-LIKE PROTEIN H.sapiens
-3.14	Hs.190616 ESTs
-3.14	Hs.12142 WD repeat domain 13

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

-3.13	Hs.249216 H2B histone family, member J
-3.13	Hs.5378 spondin 1, (f-spondin) extracellular matrix protein
-3.13	Hs.288697 hypothetical protein MGC11349
-3.12	Hs.48269 vaccinia related kinase 1
-3.11	Hs.267263 hypothetical protein
-3.11	Hs.81505 KIAA0579 protein
-3.09	Hs.9857 carbonyl reductase
-3.07	Hs.184938 Novel human gene mapping to chomosome 13
-3.06	Hs.36972 CD7 antigen (p41)
-3.04	Hs.6179 DEADH (Asp-Glu-Ala-AspHis) box polypeptide 17 (72kD)
-3.03	Hs.248007 Human beta-cytoplasmic actin (ACTBP9) pseudogene
-3.03	Hs.194637 BANP homolog, SMAR1 homolog
-2.99	Hs.61712 pyruvate dehydrogenase kinase, isoenzyme 1
-2.98	Hs.26471 Homo sapiens clone HQ0692
-2.98	Hs.292998 ESTs
-2.97	Hs.107164 spectrin, beta, non-erythrocytic 1
-2.97	Hs.94392 LDL induced EC protein
-2.95	Hs.278503 regulated in glioma
-2.95	Hs.168625 androgen-induced prostate proliferative shutoff associated protein
-2.93	Hs.81424 ubiquitin-like 1 (sentrin)
-2.91	Hs.104916 hypothetical protein FLJ21940
-2.90	Hs.99918 carboxyl ester lipase (bile salt-stimulated lipase)
-2.90	Hs.83347 angio-associated, migratory cell protein
-2.89	Hs.86178 M-phase phosphoprotein 9
-2.84	Hs.251410 Homo sapiens chromosome 19, cosmid R31180
-2.84	Hs.278741 UDP glycosyltransferase 1 family, polypeptide A8
-2.82	Hs.288617 hypothetical protein FLJ22621
-2.82	Hs.2558 bone gamma-carboxyglutamate (gla) protein (osteocalcin)
-2.81	Hs.170307 Ral guanine nucleotide exchange factor RalGPS1A
-2.81	Hs.241558 ariadne (Drosophila) homolog 2
-2.80	Hs.272317 Homo sapiens mRNA; cDNA DKFZp434O0213 (from clone DKFZp434O0213); partial cds
-2.80	Hs.293334 ESTs
-2.78	Hs.3080 mitogen-activated protein kinase 7
-2.78	Hs.94037 hypothetical protein FLJ23053
-2.78	KIAA0280 protein
-2.77	Hs.12328 KIAA1005 protein
-2.76	Hs.237825 signal recognition particle 72kD
-2.76	Hs.272792 hypothetical protein FLJ20307
-2.73	Hs.132753 F-box only protein 2
-2.71	Hs.74519 primase, polypeptide 2A (58kD)
-2.71	Hs.180338 tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein)
-2.68	Hs.285005 mitochondrial import receptor Tom22
-2.68	Hs.172052 serinethreonine kinase 18
-2.68	Hs.180903 hypothetical protein 384D8_6
-2.67	Hs.9071 progesterone membrane binding protein
-2.64	Hs.18443 aldehyde dehydrogenase 8 family, member A1
-2.63	Hs.174185 ectonucleotide pyrophosphatasephosphodiesterase 2 (autotaxin)
-2.62	Hs.17883 protein phosphatase 1G (formerly 2C), magnesium-dependent, gamma isoform
-2.62	Hs.170482 myosin, light polypeptide 5, regulatory
-2.61	Hs.180338 tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein)
-2.61	Hs.153293 KIAA0701 protein
-2.60	Hs.238272 inositol 1,4,5-triphosphate receptor, type 2
-2.59	Hs.58362 hypothetical protein FLJ12681
-2.59	Homo sapiens chromosome 19, cosmid R28784, complete sequence.
-2.58	Hs.75813 polycystic kidney disease 1 (autosomal dominant)
-2.57	Hs.23964 sin3-associated polypeptide, 18kD

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

-2.54	Hs.283675 NPD009 protein
-2.54	Hs.183887 hypothetical protein FLJ22104
-2.53	Hs.80741 propionyl Coenzyme A carboxylase, alpha polypeptide
-2.52	Hs.80828 keratin 1 (epidermolytic hyperkeratosis)
-2.52	Hs.147587 Homo sapiens mRNA; cDNA DKFZp547F134 (from clone DKFZp547F134)
-2.52	Hs.287444 hypothetical protein FLJ11722
-2.51	Hs.17409 cysteine-rich protein 1 (intestinal)
-2.50	Hs.325520 Homo sapiens IMAA mRNA for hLAT1-3TM, complete cds
-2.49	Hs.301011 KIAA0876 protein
-2.48	Hs.16193 Homo sapiens mRNA; cDNA DKFZp586B211 (from clone DKFZp586B211)
-2.48	Hs.32942 phosphoinositide-3-kinase, catalytic, gamma polypeptide
-2.48	Hs.23240 Homo sapiens cDNA FLJ13496 fis, clone PLACE1004471, weakly similar to ZINC FINGER PROTEIN 83
-2.47	Hs.23796 odz (odd Ozten-m, Drosophila) homolog 1
-2.46	Hs.180338 tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein)
-2.46	Hs.175941 B-cell receptor-associated protein BAP29
-2.44	Hs.57856 PFTAIRE protein kinase 1
-2.43	Hs.115537 putative dipeptidase
-2.43	Hs.155546 KIAA1080 protein; Golgi-associated, gamma-adaptin ear containing, ARF-binding protein 2
-2.40	Hs.20019 hemochromatosis
-2.40	Hs.207805 Homo sapiens mRNA; cDNA DKFZp564I066 (from clone DKFZp564I066)
-2.39	Hs.29725 hypothetical protein FLJ13197
-2.39	Hs.158654 KIAA1196 protein
-2.39	Hs.126779 KIAA0752 protein
-2.38	Hs.248572 hypothetical protein FLJ22965
-2.38	Hs.77152 minichromosome maintenance deficient (S. cerevisiae) 7
-2.37	Hs.91816 hypothetical protein
-2.35	Hs.95697 liver-specific bHLH-Zip transcription factor
-2.34	Hs.283978 Homo sapiens PRO2751 mRNA, complete cds
-2.34	Hs.306211 small EDRK-rich factor 1B (centromeric)
-2.33	Hs.6700 /len=604
-2.32	Hs.5022 imprinted in Prader-Willi syndrome
-2.32	Hs.82919 cullin 2
-2.31	Hs.274131 Down syndrome critical region gene 1-like 2
-2.30	Hs.7594 solute carrier family 2 (facilitated glucose transporter), member 3
-2.29	gb:NM_030900.1 /DEF=Homo sapiens KIAA0948 protein (KIAA0948), mRNA.
-2.29	Hs.271699 polymerase (DNA directed) iota
-2.29	Hs.134729 FXYD domain-containing ion transport regulator 7
-2.28	Hs.180408 solute carrier family 25 (mitochondrial carrier; Graves disease autoantigen), member 16
-2.28	Hs.57553 tousled-like kinase 2
-2.28	Hs.82919 cullin 2
-2.27	Hs.34012 breast cancer 2, early onset
-2.24	Hs.202276 KIAA1009 protein
-2.23	Hs.89563 nuclear cap binding protein subunit 1, 80kD
-2.22	Hs.966 coilin
-2.22	Hs.25155 neuroepithelial cell transforming gene 1
-2.21	Hs.108779 DKFZP586E1519 protein
-2.21	Hs.79440 IGF-II mRNA-binding protein 3
-2.20	Hs.46465 T-cell, immune regulator 1
-2.20	Hs.74861 activated RNA polymerase II transcription cofactor 4
-2.19	Hs.238944 hypothetical protein FLJ10631
-2.19	Hs.279902 cofactor required for Sp1 transcriptional activation, subunit 9 (33kD)
-2.19	Hs.79372 retinoid X receptor, beta
-2.19	Hs.183291 zinc finger protein 268
-2.19	Hs.247817 H2B histone family, member A
-2.18	Hs.274336 carnitine palmitoyltransferase II
-2.18	Hs.283709 lipopolysaccharide specific response-7 protein

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

-2.18	Hs.5541 ATPase, Ca++ transporting, ubiquitous
-2.17	Hs.8173 hypothetical protein FLJ10803
-2.16	Hs.16079 hypothetical protein FLJ10233
-2.14	Hs.180338 tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein)
-2.13	Hs.82129 carbonic anhydrase III, muscle specific
-2.13	Hs.143131 glycoprotein A33 (transmembrane)
-2.13	Hs.111244 hypothetical protein
-2.12	Hs.168640 ankylosis, progressive (mouse) homolog
-2.11	Hs.293495 ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens
-2.11	Hs.5997 hypothetical protein FLJ13078
-2.11	Hs.7995 /len=469
-2.10	Hs.519 WW domain-containing oxidoreductase
-2.10	Hs.2815 POU domain, class 6, transcription factor 1
-2.09	Hs.278985 hypothetical protein
-2.09	Hs.89474 ADP-ribosylation factor 6
-2.08	Hs.301114 zinc finger protein 79 (pT7)
-2.08	Hs.235445 hypothetical protein FLJ21313
-2.07	Hs.139033 paternally expressed 3
-2.07	Hs.62187 phosphatidylinositol glycan, class K
-2.06	Hs.109655 sex comb on midleg (Drosophila)-like 1
-2.06	Hs.279777 hypothetical protein
-2.06	Hs.75694 mannose phosphate isomerase
-2.05	Hs.5378 spondin 1, (f-spondin) extracellular matrix protein
-2.05	Hs.66180 nucleosome assembly protein 1-like 2
-2.05	Hs.306292 Homo sapiens mRNA; cDNA DKFZp564F133 (from clone DKFZp564F133)
-2.04	Hs.42215 protein phosphatase 1, regulatory subunit 6
-2.04	Hs.75574 mitochondrial ribosomal protein L19
-2.04	Hs.301512 nuclear mitotic apparatus protein 1
-2.04	Hs.58593 general transcription factor IIF, polypeptide 2 (30kD subunit)
-2.04	Hs.16193 Homo sapiens mRNA; cDNA DKFZp586B211 (from clone DKFZp586B211)
-2.03	Hs.283753 cell cycle progression 8 protein
-2.03	Hs.226103 Homo sapiens mRNA; cDNA DKFZp564G222 (from clone DKFZp564G222)
-2.03	Hs.100932 transcription factor 17
-2.03	Hs.278398 KIAA1117 protein
-2.03	Hs.39733 postsynaptic protein CRIPT
-2.03	Hs.200595 KIAA0562 gene product
-2.03	Hs.31659 thyroid hormone receptor-associated protein, 95-kD subunit
-2.03	Hs.98571 complement C1r-like proteinase precursor,
-2.02	Hs.179507 KIAA0779 protein
-2.02	Hs.71168 Homo sapiens clone 24674 mRNA sequence
-2.02	Hs.82143 E74-like factor 2 (ets domain transcription factor)
-2.02	Hs.62 protein tyrosine phosphatase, non-receptor type 12
-2.02	Hs.236642 3-hydroxyisobutyryl-Coenzyme A hydrolase
-2.02	Hs.9456 SWISNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5
-2.01	Hs.182595 dynein, axonemal, light polypeptide 4
-2.01	Hs.294014 ESTs
-2.01	Hs.920 modulator recognition factor I
-2.00	Hs.108947 KIAA0050 gene product
-2.00	Hs.111373 KIAA0423 protein
-2.00	Hs.158205 basic leucine zipper nuclear factor 1 (JEM-1)
-2.00	Hs.79078 MAD2 (mitotic arrest deficient, yeast, homolog)-like 1
-2.00	Hs.13421 KIAA0056 protein
-2.00	Hs.155995 KIAA0643 protein
-1.99	Hs.323950 zinc finger protein 6 (CMPX1)
-1.99	Hs.103834 hypothetical protein MGC5576
-1.99	Hs.300741 sorcin

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

-1.99	gb:NM_030794.1 /DEF=Homo sapiens hypothetical protein FLJ21007 (FLJ21007), mRNA.
-1.99	Hs.27413 adaptor protein containing pH domain, PTB domain and leucine zipper motif
-1.98	Hs.152151 plakophilin 4
-1.98	Hs.300684 calcitonin gene-related peptide-receptor component protein
-1.98	Hs.307091 Homo sapiens ARTS protein (PNUTL2) mRNA, complete cds; nuclear gene for mitochondrial product
-1.98	Hs.119274 RAS p21 protein activator (GTPase activating protein) 3 (Ins(1,3,4,5)P4-binding protein)
-1.98	Hs.139271 phosphodiesterase 5A, cGMP-specific
-1.98	Hs.99491 RAS guanyl releasing protein 2 (calcium and DAG-regulated)
-1.97	Hs.79368 epithelial membrane protein 1
-1.97	Hs.7627 CGI-60 protein
-1.97	Hs.265561 CD2-associated protein
-1.97	Hs.58362 /len=594
-1.97	Hs.192966 KIAA0265 protein
-1.96	Hs.288411 ESTs
-1.96	Hs.3530 TLS-associated serine-arginine protein 2
-1.95	gb:AF019888.1 /DEF=Homo sapiens Arp23 complex 20 kDa subunit (ARC20) mRNA, complete cds.
-1.95	Hs.285848 KIAA1454 protein
-1.95	Hs.105633 hypothetical protein FLJ10583
-1.95	Hs.279761 HSPC134 protein
-1.94	Hs.6217 Homo sapiens cDNA FLJ12521 fis, clone NT2RM2001840
-1.94	Hs.50335 cytochrome P450 monooxygenase
-1.92	Hs.279842 HSPC157 protein
-1.92	Hs.84560 hypothetical protein FLJ11795
-1.92	Hs.283978 Homo sapiens PRO2751 mRNA, complete cds
-1.91	Hs.25245 hypothetical protein FLJ11269
-1.91	Hs.21497 Homo sapiens, clone IMAGE:3629896, mRNA, partial cds
-1.90	Hs.178011 hypothetical protein FLJ20257
-1.90	Hs.22549 hypothetical protein FLJ12799
-1.89	Hs.3945 CGI-107 protein
-1.89	Hs.280666 Homo sapiens chromosome 19, cosmid R32184
-1.88	Hs.7158 DKFZP566H073 protein
-1.88	Hs.100729 KIAA0692 protein
-1.88	Hs.153489 ASB-1 protein
-1.88	Hs.121128 BCR downstream signaling 1
-1.88	Hs.75887 coatomer protein complex, subunit alpha
-1.87	Hs.301997 hypothetical protein FLJ13033
-1.87	Hs.71746 hypothetical protein FLJ11583
-1.87	Hs.7194 CGI-74 protein
-1.86	Human clone 23719 mRNA sequence
-1.86	Hs.234898 /len=382
-1.86	Hs.190488 hypothetical protein FLJ10120
-1.86	Hs.164036 Homo sapiens AKAP350C mRNA sequence, alternatively spliced
-1.85	Hs.79018 chromatin assembly factor 1, subunit A (p150)
-1.85	Hs.9629 papillary renal cell carcinoma (translocation-associated)
-1.85	Hs.156667 KIAA1536 protein
-1.85	Hs.87 retinoblastoma-like 1 (p107)
-1.84	Hs.100602 MAD (mothers against decapentaplegic, Drosophila) homolog 7
-1.84	Hs.6113 staufen (Drosophila, RNA-binding protein)
-1.84	Hs.8124 PH domain containing protein in retina 1
-1.83	Hs.287391 Homo sapiens chromosome 19, cosmid F23269
-1.82	Hs.166204 PHD finger protein 1
-1.82	Hs.193163 bridging integrator 1
-1.81	Hs.48291 phosphodiesterase 6D, cGMP-specific, rod, delta
-1.81	Hs.75546 capping protein (actin filament) muscle Z-line, alpha 2
-1.81	Hs.68398 period (Drosophila) homolog 1
-1.81	Hs.29956 KIAA0460 protein
-1.80	Hs.82664 ETAA16 protein

FIGURE 4

Table 2
Differential Gene Expression in Fugetaxis vs Chemotaxis SDF-1 Gradients

-1.80	Hs.153498 chromosome 18 open reading frame 1
-1.80	Hs.52463 KIAA0966 protein
-1.80	Hs.153636 far upstream element (FUSE) binding protein 3
-1.80	Hs.2780 jun D proto-oncogene
-1.79	Hs.7432 hypothetical protein FLJ10477
-1.79	Hs.24284 ADP-ribosyltransferase (NAD+; poly (ADP-ribose) polymerase)-like 2
-1.78	Hs.44131 KIAA0974 protein
-1.78	Hs.288986 survival of motor neuron 1, telomeric
-1.78	Hs.283609 hypothetical protein PRO2032
-1.78	Hs.1602 dihydropyrimidine dehydrogenase
-1.77	Hs.52891 hypothetical protein PRO1853
-1.77	Hs.326528 phosphodiesterase 3B, cGMP-inhibited
-1.77	Hs.210546 interleukin 21 receptor
-1.77	Hs.100914 hypothetical protein FLJ10352
-1.76	Hs.47099 hypothetical protein FLJ21212
-1.76	Hs.84429 KIAA0971 protein
-1.76	Hs.118194 RNA lariat debranching enzyme
-1.76	Hs.279785 putative secreted protein
-1.76	Hs.46903 hypothetical protein FLJ12838
-1.76	Hs.278857 heterogeneous nuclear ribonucleoprotein H2 (H)
-1.75	Hs.83636 adrenergic, beta, receptor kinase 1
-1.75	Hs.236642 3-hydroxyisobutyryl-Coenzyme A hydrolase
-1.75	Hs.19904 cystathionase (cystathionine gamma-lyase)
-1.74	Hs.106843 /len=765
-1.74	Hs.13225 UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 4
-1.74	Hs.151461 embryonic ectoderm development
-1.74	Hs.203772 FSHD region gene 1
-1.74	Hs.8198 zinc finger protein 204
-1.73	Hs.102456 survival of motor neuron protein interacting protein 1
-1.73	Hs.295923 seven in absentia (Drosophila) homolog 1
-1.73	Hs.16951 DKFZP586P2219 protein
-1.73	Hs.9196 hypothetical protein
-1.73	Hs.322645 Homo sapiens mRNA; cDNA DKFZp586J101 (from clone DKFZp586J101)
-1.73	Hs.239934 CGI-96 protein
-1.72	Hs.22559 KIAA0197 protein
-1.72	Hs.112493 Homo sapiens mRNA; cDNA DKFZp564D036 (from clone DKFZp564D036)
-1.72	Hs.26102 trichorhinophalangeal syndrome I
-1.72	Hs.252723 ribosomal protein L19
-1.72	Hs.244 amino-terminal enhancer of split
-1.72	Hs.279819 APR-1 protein
-1.71	Hs.295446 ESTs, Moderately similar to 810024C cytochrome oxidase I H.sapiens
-1.71	Hs.30696 transcription factor-like 5 (basic helix-loop-helix)
-1.71	Hs.31834 Homo sapiens clone 25129 mRNA sequence
-1.71	Hs.14928 hypothetical protein FLJ12903
-1.71	Hs.236940 /len=570
-1.71	Hs.48433 endocrine regulator
-1.71	Hs.283912 Homo sapiens PAC clone RP4-771P4 from 7q11.21-q11.23
-1.71	Hs.129445 hypothetical protein FLJ12496
-1.70	Hs.49526 f-box and leucine-rich repeat protein 4
-1.70	Hs.70359 KIAA0136 protein
-1.70	Hs.75790 phosphatidylinositol glycan, class C
-1.70	Hs.83790 KIAA0305 gene product
-1.70	Hs.18885 CGI-116 protein
-1.70	Hs.232068 transcription factor 8 (represses interleukin 2 expression)

FIGURE 5

Table 3
Differential Gene Expression in Chemokinesis vs Chemotaxis SDF-1 Gradients

UP REGULATED IN CHEMOTAXIS COMPARED TO CHEMOKINESIS SDF-1 GRADIENTS

80.37	Hs.99120 DEADH (Asp-Glu-Ala-AspHis) box polypeptide, Y chromosome
51.46	Hs.80358 SMC (mouse) homolog, Y chromosome
36.38	Hs.180911 ribosomal protein S4, Y-linked
24.62	Hs.155103 eukaryotic translation initiation factor 1A, Y chromosome
21.08	Hs.193145 ubiquitin specific protease 9, Y chromosome (Drosophila fat facets related)
16.17	Hs.155397 Homo sapiens mRNA; cDNA DKFZp564K143 (from clone DKFZp564K143)
12.68	Hs.177605 killer cell lectin-like receptor subfamily C, member 2
11.67	Hs.75658 phosphorylase, glycogen; brain
10.31	Hs.155103 eukaryotic translation initiation factor 1A, Y chromosome
9.31	Hs.301636 peroxisomal biogenesis factor 6
9.28	Hs.99120 DEADH (Asp-Glu-Ala-AspHis) box polypeptide, Y chromosome
8.95	FK506-binding protein 8 (38kD)
8.15	Hs.37427 erythrocyte membrane protein band 4.1 (elliptocytosis 1, RH-linked)
7.92	Hs.278599 nuclear receptor subfamily 6, group A, member 1
6.60	Hs.25817 BTB (POZ) domain containing 2
6.45	Hs.79410 solute carrier family 4, anion exchanger, member 2 (erythrocyte membrane protein band 3-like 1)
6.13	Hs.56336 protein kinase, Y-linked
6.10	Hs.5541 ATPase, Ca++ transporting, ubiquitous
6.04	Hs.180577 granulin
5.26	Hs.73931 major histocompatibility complex, class II, DQ beta 1
5.01	Hs.10306 natural killer cell group 7 sequence
4.63	Hs.272108 ESTs
4.28	Hs.121073 hypothetical protein FLJ10466
4.27	Hs.79340 PTH-responsive osteosarcoma B1 protein
4.19	Hs.89560 iduronidase, alpha-L-
3.91	Hs.272438 discs, large (Drosophila) homolog 3 (neuroendocrine-dlg)
3.90	Hs.104555 neuropeptide FF-amide peptide precursor
3.79	Hs.285753 SCG10-like-protein
3.75	Hs.99877 Janus kinase 3 (a protein tyrosine kinase, leukocyte)
3.56	Hs.187378 hypothetical protein FLJ11278
3.54	Hs.58362 hypothetical protein FLJ12681
3.40	Hs.98614 ribosome binding protein 1 (dog 180kD homolog)
3.38	Hs.12142 WD repeat domain 13
3.35	Hs.202672 endothelial differentiation, sphingolipid G-protein-coupled receptor, 5
3.35	Hs.41 carcinoembryonic antigen-related cell adhesion molecule 8
3.31	Hs.76415 inter-alpha (globulin) inhibitor H4 (plasma Kallikrein-sensitive glycoprotein)
3.21	Hs.326035 early growth response 1
3.18	Hs.193324 ESTs
3.17	Hs.279651 melanoma inhibitory activity
3.13	Hs.194662 calponin 3, acidic
3.13	Hs.167380 BLu protein
3.10	Hs.181353 UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2
3.10	Hs.110964 hypothetical protein FLJ23471
3.10	Hs.147472 dynein intermediate chain 2
3.09	Hs.7724 KIAA0963 protein
3.03	gb:U52696.1 /DEF=Human adrenal Creb-rp homolog (Creb-rp), complete cds, and tenascin-X (XB), partial cds, mRNA.
3.02	Hs.134729 FXYD domain-containing ion transport regulator 7
2.99	Hs.17409 cysteine-rich protein 1 (intestinal)
2.95	Hs.3066 granzyme K (serine protease, granzyme 3; tryptase II)
2.90	Hs.92381 nudix (nucleoside diphosphate linked moiety X)-type motif 4
2.90	Hs.242407 G protein-coupled receptor, family C, group 5, member B
2.86	Hs.76289 biliverdin reductase B (flavin reductase (NADPH))
2.84	Hs.7258 hypothetical protein FLJ22021
2.84	gb:NM_030931.1 /DEF=Homo sapiens epididymal secretory protein ESP13.2 (ESP13.2), mRNA.
2.82	Hs.233789 ESTs
2.81	Hs.64096 KIAA0427 gene product

FIGURE 5

Table 3
Differential Gene Expression in Chemokinesis vs Chemotaxis SDF-1 Gradients

2.78	Hs.328822 haptoglobin-related protein
2.76	Hs.247950 H.sapiens mRNA for Ig light chain, variable region (ID:CLL001VL)
2.75	Hs.248 mitogen-activated protein kinase kinase kinase 8
2.75	Hs.272891 hippocalcin-like protein 4
2.74	Hs.72964 makorin, ring finger protein, 3
2.65	Hs.234642 aquaporin 3
2.64	Hs.85112 insulin-like growth factor 1 (somatomedin C)
2.60	Hs.306425 Homo sapiens mRNA for KIAA1417 protein, partial cds
2.60	Hs.321149 hypothetical protein FLJ10257
2.55	Hs.306412 Homo sapiens cDNA FLJ20854 fis, clone ADKA01341
2.54	Hs.278932 PRO0214 protein
2.51	Hs.192662 hypothetical protein FLJ10469
2.49	Hs.283675 NPD009 protein
2.48	Hs.12229 TGFB inducible early growth response 2
2.47	Hs.160318 FXYD domain-containing ion transport regulator 1 (phospholemman)
2.47	Hs.300711 annexin A5
2.46	Hs.171825 basic helix-loop-helix domain containing, class B, 2
2.44	Hs.112434 Novel human gene mapping to chomosome 13
2.43	Hs.81182 histamine N-methyltransferase
2.43	Hs.144630 nuclear receptor subfamily 2, group F, member 1
2.41	Hs.66718 RAD54 (S.cerevisiae)-like
2.41	Hs.211388 Homo sapiens BAC clone CTB-60N22 from 7q21
2.40	Hs.250870 mitogen-activated protein kinase kinase 5
2.35	Hs.24083 KIAA0997 protein
2.34	Hs.30250 v-maf musculoaponeurotic fibrosarcoma (avian) oncogene homolog
2.33	Hs.78995 MADS box transcription enhancer factor 2, polypeptide C (myocyte enhancer factor 2C)
2.32	Hs.83169 matrix metalloproteinase 1 (interstitial collagenase)
2.32	Hs.36972 CD7 antigen (p41)
2.30	Hs.7627 CGI-60 protein
2.30	Hs.61258 argininosuccinate lyase
2.29	Hs.184915 zinc finger protein, Y-linked
2.27	Hs.105700 secreted frizzled-related protein 4
2.24	Hs.9688 leukocyte membrane antigen
2.22	Hs.5881 ELL gene (11-19 lysine-rich leukemia gene)
2.19	Human DNA sequence from clone RP5-1174N9 on chromosome 1p34.1-35.3. Contains the gene for a novel protein with IBR domain, a (pseudo
2.18	Hs.94970 KIAA0306 protein
2.18	Hs.322422 Homo sapiens cDNA FLJ11676 fis, clone HEMBA1004752, highly similar to Homo sapiens mRNA for LAK-4p
2.17	Hs.195464 filamin A, alpha (actin-binding protein-280)
2.16	gb:NM_030753.1 /DEF=Homo sapiens wingless-type MMTV integration site family, member 3 (WNT3), mRNA.
2.15	Hs.195432 aldehyde dehydrogenase 2 family (mitochondrial)
2.15	Hs.1724 interleukin 2 receptor, alpha
2.14	Hs.21497 Homo sapiens, clone IMAGE:3629896, mRNA, partial cds
2.09	Hs.36972 CD7 antigen (p41)
2.08	Hs.11590 cathepsin F
2.08	Hs.57749 synaptic nuclei expressed gene 2; KIAA1011 protein
2.07	Hs.103382 phospholipid scramblase 3
2.06	Hs.77858 mesenchyme homeo box 2 (growth arrest-specific homeo box)
2.06	Hs.64239 Human DNA sequence from clone RP5-1174N9 on chromosome 1p34.1-35.3. Contains the gene for a novel protein with IBR domain, a (pseudo
2.06	Hs.211584 neurofilament, light polypeptide (68kD)
2.05	Hs.278295 cholinergic receptor, nicotinic, epsilon polypeptide
2.05	Hs.11809 single Ig IL-1R-related molecule
2.04	Hs.3838 serum-inducible kinase
2.03	aquaporin 3
2.02	Hs.307091 Homo sapiens ARTS protein (PNUTL2) mRNA, complete cds; nuclear gene for mitochondrial product
1.99	Hs.71746 hypothetical protein FLJ11583

FIGURE 5

Table 3
Differential Gene Expression in Chemokinesis vs Chemotaxis SDF-1 Gradients

1.98	Hs.58362 /len=594
1.97	Hs.195464 filamin A, alpha (actin-binding protein-280)
1.96	Hs.81256 S100 calcium-binding protein A4 (calcium protein, calvasculin, metastasin, murine placental homolog)
1.96	Hs.79019 baculoviral IAP repeat-containing 1
1.95	Hs.78781 vascular endothelial growth factor B
1.94	Hs.7019 signal-induced proliferation-associated gene 1
1.94	Hs.68877 cytochrome b-245, alpha polypeptide
1.94	Hs.195464 filamin A, alpha (actin-binding protein-280)
1.92	Hs.1103 transforming growth factor, beta 1
1.92	Hs.150540 Homo sapiens, clone IMAGE:3954961, mRNA, partial cds
1.90	Hs.155191 villin 2 (ezrin)
1.90	Hs.301417 AHNAK nucleoprotein (desmoyokin)
1.90	Hs.112049 SET binding factor 1
1.88	Hs.73956 NAD(P)H menadione oxidoreductase 2, dioxin-inducible
1.88	Hs.202687 potassium voltage-gated channel, Shal-related subfamily, member 2
1.88	Hs.5345 arginyl aminopeptidase (aminopeptidase B)-like 1
1.88	Hs.30127 hypothetical protein
1.86	Hs.7252 KIAA1224 protein
1.85	Hs.76240 adenylate kinase 1
1.85	Hs.25999 hypothetical protein FLJ22195
1.84	Hs.118463 transport-secretion protein 2.2,
1.84	Hs.153529 Homo sapiens clone 24540 mRNA sequence
1.82	Hs.9999 epithelial membrane protein 3
1.82	Hs.167017 gamma-aminobutyric acid (GABA) B receptor, 1
1.82	Hs.51305 v-maf musculoaponeurotic fibrosarcoma (avian) oncogene family, protein F
1.82	Hs.272972 hypothetical protein FLJ20185
1.81	peroxisomal biogenesis factor 6
1.81	Hs.103147 hypothetical protein FLJ21347
1.80	Hs.74573 similar to vaccinia virus HindIII K4L ORF
1.80	Hs.62402 p21Cdc42Rac1-activated kinase 1 (yeast Ste20-related)
1.80	Hs.112028 MisshapenNIK-related kinase
1.79	Hs.428 fms-related tyrosine kinase 3 ligand
1.78	Hs.100071 6-phosphogluconolactonase
1.77	Hs.99491 RAS guanyl releasing protein 2 (calcium and DAG-regulated)
1.76	Hs.182982 golgin-67
1.76	Hs.31659 thyroid hormone receptor-associated protein, 95-kD subunit
1.75	Hs.275438 histone deacetylase 7A
1.74	Hs.2551 adrenergic, beta-2-, receptor, surface
1.74	Hs.91299 guanine nucleotide binding protein (G protein), beta polypeptide 2
1.73	Hs.11809 /len=525
1.73	Hs.9731 nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, beta
1.73	Hs.195484 Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 327506
1.73	Hs.180040 hypothetical protein FLJ22439
1.72	Hs.94382 adenosine kinase
1.72	Hs.156667 KIAA1536 protein
1.72	Hs.285313 core promoter element binding protein
1.72	Hs.47344 advillin
1.72	Hs.41502 hypothetical protein FLJ21276
1.71	Hs.7647 MYC-associated zinc finger protein (purine-binding transcription factor)
1.71	Hs.104481 Nck, Ash and phospholipase C binding protein
1.71	Hs.178011 hypothetical protein FLJ20257
1.70	Hs.131885 /len=582
1.70	Hs.108947 KIAA0050 gene product
1.70	Hs.272814 hypothetical protein DKFZp434E1723

FIGURE 5

Table 3
Differential Gene Expression in Chemokinesis vs Chemotaxis SDF-1 Gradients

DOWN REGULATED IN CHEMOTAXIS COMPARED TO CHEMOKINESIS SDF-1 GRADIENTS

-17.85	Hs.223014 antizyme inhibitor
-12.91	Hs.76364 allograft inflammatory factor 1
-5.81	Hs.82985 collagen, type V, alpha 2
-5.69	Hs.7358 hypothetical protein FLJ13110
-5.42	Hs.212587 Homo sapiens mRNA; cDNA DKFZp566M043 (from clone DKFZp566M043)
-5.06	Hs.51120 cathelicidin antimicrobial peptide
-4.80	Hs.173464 FK506-binding protein 8 (38kD)
-4.69	Hs.134503 PR domain containing 8
-4.54	Hs.119500 ribosomal protein, large P2
-4.27	Hs.139263 calcium channel, voltage-dependent, alpha 1F subunit
-4.24	Hs.76845 phosphoserine phosphatase-like
-4.23	Hs.182740 ribosomal protein S11
-4.18	gb:M24668.1 /DEF=Human Ig rearranged H-chain V-region mRNA (C-D-JH4), complete cds.
-3.89	Hs.73793 vascular endothelial growth factor
-3.89	Hs.75105 emopamil-binding protein (sterol isomerase)
-3.86	Hs.274 megakaryocyte-associated tyrosine kinase
-3.86	Hs.24322 ATPase, H+ transporting, lysosomal (vacuolar proton pump) 9kD
-3.78	Hs.203269 ESTs, Moderately similar to ALU8_HUMAN ALU SUBFAMILY SX SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens
-3.76	Hs.3112 sodium channel, nonvoltage-gated 1, gamma
-3.72	Hs.10247 activated leucocyte cell adhesion molecule
-3.67	Hs.406 solute carrier family 6 (neurotransmitter transporter, dopamine), member 3
-3.66	Hs.27184 growth factor, erv1 (S. cerevisiae)-like (augmenter of liver regeneration)
-3.63	Hs.321223 keratin 6B
-3.57	Hs.173594 serine (or cysteine) proteinase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 1
-3.52	Hs.152251 frizzled (Drosophila) homolog 5
-3.50	Hs.69752 desmocollin 1
-3.48	Hs.159581 matrix metalloproteinase 17 (membrane-inserted)
-3.48	Hs.105927 stem cell growth factor; lymphocyte secreted C-type lectin
-3.47	Hs.223241 eukaryotic translation elongation factor 1 delta (guanine nucleotide exchange protein)
-3.40	Hs.24322 ATPase, H+ transporting, lysosomal (vacuolar proton pump) 9kD
-3.36	Hs.239737 C-terminal binding protein 1
-3.33	Hs.78305 RAB2, member RAS oncogene family
-3.32	Hs.84285 ubiquitin-conjugating enzyme E2I (homologous to yeast UBC9)
-3.29	Hs.303649 small inducible cytokine A2 (monocyte chemotactic protein 1, homologous to mouse Sig-je)
-3.27	Hs.183362 hypothetical protein FLJ20535
-3.26	Hs.146409 cell division cycle 42 (GTP-binding protein, 25kD)
-3.22	Hs.2969 v-ski avian sarcoma viral oncogene homolog
-3.20	Hs.279832 hypothetical protein FLJ10488
-3.18	Hs.187354 nuclear receptor subfamily 2, group E, member 3
-3.16	Hs.66578 corticotropin releasing hormone receptor 2
-3.12	Hs.19280 cysteine-rich motor neuron 1
-3.12	Hs.154999 ESTs, Moderately similar to HERC2 H.sapiens
-3.11	Hs.273294 hypothetical protein FLJ20069
-3.10	Hs.139137 Homo sapiens clone 24442 mRNA sequence
-3.06	Hs.178749 synovial sarcoma, X breakpoint 3
-3.06	Hs.7645 fibrinogen, B beta polypeptide
-3.05	Hs.154085 leucine zipper protein 1
-3.04	Hs.198427 hexokinase 2
-3.03	Hs.302022 PR domain containing 16
-3.01	Hs.105859 hypothetical protein FLJ10260
-2.98	Hs.278581 fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)
-2.98	Hs.278581 fibroblast growth factor receptor 2 (bacteria-expressed kinase, keratinocyte growth factor receptor, craniofacial dysostosis 1, Crouzon syndrome, Pfeiffer syndrome, Jackson-Weiss syndrome)
-2.98	Hs.4775 junctophilin 3

FIGURE 5

Table 3
Differential Gene Expression in Chemokinesis vs Chemotaxis SDF-1 Gradients

-2.95	Hs.82280 regulator of G-protein signalling 10
-2.95	Hs.225170 hypothetical protein FLJ11535
-2.92	Hs.125783 DEME-6 protein
-2.92	gb:BC006196.1 /DEF=Homo sapiens, tumor necrosis factor receptor superfamily, member 9, clone MGC:2172, mRNA, complete cds.
-2.92	Hs.16488 calreticulin
-2.92	Hs.292911 ESTs
-2.91	Hs.142907 Human BRCA2 region, mRNA sequence CG011
-2.89	Hs.306778 Homo sapiens cDNA: FLJ21524 fis, clone COL05921
-2.85	Hs.307345 Homo sapiens putative transcription factor (MTG8) mRNA, alternatively spliced, partial cds
-2.85	Hs.123062 Human mRNA for T cell receptor, clone IGRA24
-2.80	Hs.315463 suppression of tumorigenicity 16 (melanoma differentiation)
-2.78	Hs.109733 CGI-131 protein
-2.78	Hs.248190 UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 4 (GalNAc-T4)
-2.74	Hs.41752 keratin, hair, acidic,2
-2.73	Hs.1166 thrombopoietin (myeloproliferative leukemia virus oncogene ligand, megakaryocyte growth and development factor)
-2.72	Hs.159900 G protein-coupled receptor 15
-2.68	Hs.7936 BAI1-associated protein 2
-2.68	Hs.283330 hypothetical protein PRO1843
-2.67	Hs.57764 protein phosphatase 1A (formerly 2C), magnesium-dependent, alpha isoform
-2.64	Hs.115365 chromosome X open reading frame 2
-2.64	Hs.16488 calreticulin
-2.64	Hs.128311 ESTs
-2.64	Hs.283055 hypothetical protein PRO1316
-2.60	Hs.93758 H4 histone family, member H
-2.58	Hs.249727 hypothetical protein FLJ11798
-2.57	Hs.233568 H2A histone family, member I
-2.55	Hs.171995 kallikrein 3, (prostate specific antigen)
-2.55	Hs.85302 adenosine deaminase, RNA-specific, B1 (homolog of rat RED1)
-2.55	Hs.172928 collagen, type I, alpha 1
-2.54	Hs.702 cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 18
-2.53	Hs.3781 similar to murine leucine-rich repeat protein
-2.52	Hs.288650 aquaporin 4
-2.47	Hs.322680 Homo sapiens cDNA: FLJ21547 fis, clone COL06206
-2.43	Hs.69559 KIAA1096 protein
-2.42	Hs.108287 intercellular adhesion molecule 4, Landsteiner-Wiener blood group
-2.41	Hs.194765 H.sapiens GENX-5624 mRNA, 3 UTR
-2.41	Hs.213392 hypothetical protein FLJ13195 similar to stromal antigen 3
-2.41	Hs.166715 hypothetical protein PRO2533
-2.38	Hs.65149 growth hormone 2
-2.38	gb:BC005949.1 /DEF=Homo sapiens, similar to rat myomegalin, clone MGC:14586, mRNA, complete cds.
-2.38	Hs.306243 Homo sapiens thioredoxin delta 3 (TXN delta 3) mRNA, partial cds
-2.37	Hs.306602 Homo sapiens cDNA FLJ11514 fis, clone HEMBA1002229
-2.35	gb:NM_012465.1 /DEF=Homo sapiens tolloid-like 2 (TLL2), mRNA.
-2.32	Hs.41135 endomucin-2
-2.31	Hs.111732 Fc fragment of IgG binding protein
-2.31	Hs.73064 gonadotropin-releasing hormone receptor
-2.30	Hs.7306 secreted frizzled-related protein 1
-2.30	Hs.288931 Homo sapiens cDNA FLJ13034 fis, clone NT2RP3001232
-2.29	Hs.25732 eukaryotic translation initiation factor 4 gamma, 3
-2.29	gb:NM_030975.1 /DEF=Homo sapiens keratin associated protein 9.9 (KRTAP9.9), mRNA.
-2.27	Hs.20137 hypothetical protein DKFZp434P0116
-2.26	Hs.97109 ESTs
-2.23	Hs.111611 ribosomal protein L27
-2.20	Hs.78629 ATPase, Na+K+ transporting, beta 1 polypeptide
-2.19	Hs.180919 inhibitor of DNA binding 2, dominant negative helix-loop-helix protein
-2.16	Hs.4147 translocating chain-associating membrane protein

FIGURE 5

Table 3
Differential Gene Expression in Chemokinesis vs Chemotaxis SDF-1 Gradients

-2.15	Hs.183805 ankyrin 1, erythrocytic
-2.15	Hs.14846 Homo sapiens mRNA; cDNA DKFZp564D016 (from clone DKFZp564D016)
-2.14	Hs.124126 Homo sapiens clone 24438 mRNA sequence
-2.13	Hs.199538 inhibin, beta C
-2.12	Hs.301946 lymphoid blast crisis oncogene
-2.11	Hs.28777 H2A histone family, member L
-2.09	Hs.75736 apolipoprotein D
-2.09	Hs.25051 plakophilin 2
-2.09	Hs.79170 KIAA0227 protein
-2.07	Hs.142023 T cell activation, increased late expression
-2.07	Hs.305979 Homo sapiens clone FLB3024 PRO0756 mRNA, complete cds
-2.06	Hs.279773 diferentiation-related protein dif13
-2.05	Hs.2388 apolipoprotein F
-2.05	Hs.91971 cAMP-regulated guanine nucleotide exchange factor II
-2.05	Hs.3781 similar to murine leucine-rich repeat protein
-2.05	Hs.79474 tyrosine 3-monooxygenasetryptophan 5-monooxygenase activation protein, epsilon polypeptide
-2.05	Hs.133130 Homo sapiens mRNA; cDNA DKFZp566H0124 (from clone DKFZp566H0124)
-1.99	Hs.76064 ribosomal protein L27a
-1.98	Hs.75929 cadherin 11, type 2, OB-cadherin (osteoblast)
-1.97	Hs.48950 heptacellular carcinoma novel gene-3 protein
-1.96	Hs.142570 Homo sapiens clone 24629 mRNA sequence
-1.94	Hs.184245 KIAA0929 protein Msx2 interacting nuclear target (MINT) homolog
-1.94	Hs.127828 guanine nucleotide binding protein (G protein), gamma 7
-1.94	Hs.279903 Ras homolog enriched in brain 2
-1.94	Hs.42194 hypothetical protein FLJ22649 similar to signal peptidase SPC2223
-1.93	Hs.159003 transient receptor potential channel 6
-1.93	Hs.75871 protein kinase C binding protein 1
-1.92	Hs.75294 corticotropin releasing hormone
-1.92	Hs.262869 plasminogen-like
-1.90	Hs.239176 insulin-like growth factor 1 receptor
-1.90	Hs.16533 myosin phosphatase, target subunit 1
-1.89	Hs.129683 Homo sapiens unknown mRNA, sequence
-1.88	Hs.24385 Human hbc647 mRNA sequence
-1.87	Hs.165662 KIAA0675 gene product
-1.87	Hs.283037 HSPC039 protein
-1.86	Hs.152939 Homo sapiens clone 24630 mRNA sequence
-1.86	Hs.89474 ADP-ribosylation factor 6
-1.86	Hs.247904 Human DNA sequence from clone 1060K6 on chromosome 20p12.1-13 Contains a pseudogene similar to 40S ribosomal protein S11, ESTs, STSs and GSSs
-1.86	Hs.121128 BCR downstream signaling 1
-1.85	Hs.56043 CGI-115 protein
-1.84	Hs.184050 v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene homolog
-1.84	Hs.50716 hypothetical protein SIRP-b2
-1.83	Hs.133207 PTPRF interacting protein, binding protein 1 (liprin beta 1)
-1.82	Hs.7910 RING1 and YY1 binding protein
-1.81	Hs.25732 eukaryotic translation initiation factor 4 gamma, 3
-1.81	Hs.159526 patched (Drosophila) homolog
-1.81	Hs.92254 hypothetical protein FLJ20163
-1.80	Hs.56966 KIAA0906 protein
-1.80	Hs.283729 ESTs
-1.79	Hs.76884 inhibitor of DNA binding 3, dominant negative helix-loop-helix protein
-1.79	Hs.298014 Homo sapiens cDNA FLJ14136 fis, clone MAMMA1002744
-1.79	Hs.283683 chromosome 8 open reading frame 4
-1.78	Hs.115823 ribonuclease P, 40kD subunit
-1.78	Hs.292245 ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens
-1.77	Hs.17211 dedicator of cyto-kinesis 2
-1.76	Hs.69547 myelin basic protein

FIGURE 5

Table 3
Differential Gene Expression in Chemokinesis vs Chemotaxis SDF-1 Gradients

-1.76	Hs.223241 eukaryotic translation elongation factor 1 delta (guanine nucleotide exchange protein)
-1.76	Hs.150551 ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens
-1.76	Hs.73291 hypothetical protein FLJ10881
-1.75	Hs.274382 protein kinase, interferon-inducible double stranded RNA dependent
-1.75	Hs.79732 fibulin 1
-1.75	Hs.502 ATP-binding cassette, sub-family B (MDRTAP), member 3
-1.74	Hs.212587 Homo sapiens mRNA; cDNA DKFZp566M043 (from clone DKFZp566M043)
-1.72	Hs.86958 interferon (alpha, beta and omega) receptor 2
-1.72	Hs.1948 ribosomal protein S21
-1.72	Hs.293007 aminopeptidase puromycin sensitive
-1.72	Hs.173381 dihydropyrimidinase-like 2
-1.72	Hs.42409 CGI-146 protein
-1.71	Hs.1600 chaperonin containing TCP1, subunit 5 (epsilon)
-1.71	Hs.97681 DNA (cytosine-5-)-methyltransferase 2
-1.71	Hs.144931 ATPase, aminophospholipid transporter (APLT), Class I, type 8A, member 1
-1.70	Hs.288106 hypothetical protein FLJ21168
-1.70	Hs.323712 KIAA0615 gene product
-1.70	Hs.167835 acyl-Coenzyme A oxidase 1, palmitoyl
-1.70	Hs.326248 Homo sapiens cDNA: FLJ22071 fis, clone HEP11691
-1.70	Hs.180919 inhibitor of DNA binding 2, dominant negative helix-loop-helix protein

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

UP REGULATED IN FUGETAXIS COMPARED TO CHEMOKINESIS SDF-1 GRADIENTS

39.87	Hs.80358 SMC (mouse) homolog, Y chromosome
35.11	Hs.99120 DEADH (Asp-Glu-Ala-AspHis) box polypeptide, Y chromosome
33.40	Hs.180911 ribosomal protein S4, Y-linked
13.24	Hs.155397 Homo sapiens mRNA; cDNA DKFZp564K143 (from clone DKFZp564K143)
12.03	Hs.75184 chitinase 3-like 1 (cartilage glycoprotein-39)
10.64	Hs.78913 chemokine (C-X3-C) receptor 1
10.01	Hs.155103 eukaryotic translation initiation factor 1A, Y chromosome
8.19	Hs.193145 ubiquitin specific protease 9, Y chromosome (Drosophila fat facets related)
8.08	Hs.75184 chitinase 3-like 1 (cartilage glycoprotein-39)
7.64	Hs.100000 S100 calcium-binding protein A8 (calgranulin A)
6.57	Hs.10306 natural killer cell group 7 sequence
6.42	Hs.153837 myeloid cell nuclear differentiation antigen
6.10	Hs.77436 pleckstrin
5.97	Hs.99120 DEADH (Asp-Glu-Ala-AspHis) box polypeptide, Y chromosome
5.67	Hs.137583 peptidoglycan recognition protein
5.51	Hs.81665 v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog
5.36	Hs.195432 aldehyde dehydrogenase 2 family (mitochondrial)
5.26	Hs.204238 lipocalin 2 (oncogene 24p3)
5.15	Hs.123079 Glutamate transporter II variant BHBGT IIB {5 region} human, brain and spinal cord, mRNA Partial Mutant, 129 nt
4.99	Hs.301636 peroxisomal biogenesis factor 6
4.99	Hs.2962 S100 calcium-binding protein P
4.94	Hs.250700 tryptase beta 1
4.75	Hs.158303 PR domain containing 1, with ZNF domain
4.63	Hs.19413 S100 calcium-binding protein A12 (calgranulin C)
4.46	Hs.41 carcinoembryonic antigen-related cell adhesion molecule 8
4.20	Hs.76171 CCAATenhancer binding protein (CEBP), alpha
4.17	Hs.2582 defensin, alpha 4, corticostatin
4.08	Hs.155103 eukaryotic translation initiation factor 1A, Y chromosome
3.99	Hs.7724 KIAA0963 protein
3.99	Hs.130760 myosin phosphatase, target subunit 2
3.94	Hs.177605 killer cell lectin-like receptor subfamily C, member 2
3.94	Hs.258588 olfactory receptor, family 1, subfamily A, member 2
3.92	Hs.74076 CD163 antigen
3.91	Hs.286124 CD24 antigen (small cell lung carcinoma cluster 4 antigen)
3.91	Hs.181353 UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2
3.89	Hs.298469 angiotensin I converting enzyme (peptidyl-dipeptidase A) 1
3.87	Hs.273321 differentially expressed in hematopoletic lineages
3.86	Hs.13040 G protein-coupled receptor 86
3.84	Hs.18551 neuroblastoma (nerve tissue) protein
3.79	Hs.6527 G protein-coupled receptor 56
3.77	Hs.75703 small inducible cytokine A4 (homologous to mouse Mip-1b)
3.70	Hs.42346 calcineurin-binding protein calsarcin-1
3.66	Hs.287539 hypothetical protein FLJ12662
3.65	Hs.232070 telomerase-associated protein 1
3.64	Hs.233634 hypothetical protein FLJ14220
3.63	Hs.183125 killer cell lectin-like receptor F1
3.62	Hs.239500 KIAA0273 gene product
3.59	Hs.196352 neutrophil cytosolic factor 4 (40kD)
3.57	Hs.301540 sepiapterin reductase (7,8-dihydrobiopterin:NADP+ oxidoreductase)
3.55	Hs.105938 lactotransferrin
3.51	Hs.56336 protein kinase, Y-linked
3.51	Hs.294158 tryptase beta 2
3.50	Hs.621 lectin, galactoside-binding, soluble, 3 (galectin 3)
3.47	Hs.36978 melanoma antigen, family A, 3
3.45	Hs.352 folate receptor 3 (gamma)
3.45	Hs.198037 KIAA0599 protein

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

3.40	Hs.89499 arachidonate 5-lipoxygenase
3.38	Hs.57975 calsequestrin 2 (cardiac muscle)
3.35	Hs.167380 BLu protein
3.34	Hs.2621 cystatin A (stefin A)
3.34	Hs.1619 achaete-scute complex (Drosophila) homolog-like 1
3.34	Hs.8719 hypothetical protein MGC1136
3.30	Hs.129708 tumor necrosis factor (ligand) superfamily, member 14
3.29	Hs.25817 BTB (POZ) domain containing 2
3.29	Hs.172631 integrin, alpha M (complement component receptor 3, alpha; also known as CD11b (p170), macrophage antigen alpha polypeptide)
3.25	Hs.37142 ephrin-A5
3.23	Hs.127384 DKFZP564C196 protein
3.21	Hs.80248 RNA-binding protein gene with multiple splicing
3.21	Hs.242407 G protein-coupled receptor, family C, group 5, member B
3.20	Hs.248159 persephin
3.19	Hs.293266 sperm protein associated with the nucleus, X chromosome, family member A1
3.12	Hs.107716 hypothetical protein FLJ22344
3.11	Hs.139425 Homo sapiens cDNA FLJ12744 fis, clone NT2RP2000715
3.10	Hs.82112 interleukin 1 receptor, type I
3.07	Hs.785 integrin, alpha 2b (platelet glycoprotein IIb of IIbIIIa complex, antigen CD41B)
3.06	Hs.17752 phosphatidylserine-specific phospholipase A1alpha
3.03	Hs.190846 Homo sapiens GREB1b (GREB1) mRNA, complete cds, alternatively spliced
3.01	Hs.79516 brain abundant, membrane attached signal protein 1
3.00	Hs.226014 Human DNA sequence from clone 240B8 on chromosome 6p11.2-q12. Contains the 3 part of a gene for a novel protein similar to T-STAR, Etoile, Sam68, SLM1 and p62 Tyrosine Phosphoprotein. Contains ESTs, STSs, GSSs and genomic marker D6S1695
2.98	Hs.76807 major histocompatibility complex, class II, DR alpha
2.98	Hs.181128 ELK1, member of ETS oncogene family
2.98	Hs.92381 nudix (nucleoside diphosphate linked moiety X)-type motif 4
2.95	granulysin
2.94	Hs.75990 haptoglobin
2.94	Hs.2142 5-hydroxytryptamine (serotonin) receptor 3A
2.91	Hs.75260 mitogen inducible 2
2.87	Hs.181353 UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2
2.85	Hs.278528 tryptase, alpha
2.81	Hs.274562 Homo sapiens mRNA; cDNA DKFZp434E2028 (from clone DKFZp434E2028)
2.77	Hs.3195 small inducible cytokine subfamily C, member 1 (lymphotactin)
2.77	Hs.332045 Homo sapiens cDNA FLJ20161 fis, clone COL09252, highly similar to L33930 Homo sapiens CD24 signal transducer mRNA
2.76	Hs.141496 MAGE-like 2
2.75	Hs.122552 G-2 and S-phase expressed 1
2.73	Hs.164960 BarH-like homeobox 1
2.71	Hs.129706 paired box gene 4
2.70	Hs.77436 pleckstrin
2.70	Hs.119597 stearoyl-CoA desaturase (delta-9-desaturase)
2.70	Hs.130546 hypothetical protein FLJ20449
2.69	Hs.301417 AHNAK nucleoprotein (desmoyokin)
2.66	Hs.272278 cholinergic receptor, nicotinic, alpha polypeptide 9
2.64	Hs.76722 CCAATenhancer binding protein (CEBP), delta
2.64	Hs.75607 myristoylated alanine-rich protein kinase C substrate (MARCKS, 80K-L)
2.64	Hs.307177 Human SH3 domain-containing protein SH3P17 mRNA, complete cds
2.63	Hs.250696 KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3
2.61	Hs.108196 HSPC037 protein
2.60	Hs.79006 deoxythymidylate kinase (thymidylate kinase)
2.56	Hs.256986 ESTs, Moderately similar to VPP2_HUMAN VACUOLAR PROTON TRANSLOCATING ATPASE 116 KDA SUBUNIT A ISOFORM 2 H.sapiens
2.55	Hs.198003 sarcosine dehydrogenase
2.54	Hs.112259 T cell receptor gamma locus
2.52	Hs.52931 adrenergic, alpha-1A-, receptor

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

2.51	Hs.50929 hypothetical protein FLJ13842
2.50	Hs.123030 Human kappa-immunoglobulin germline pseudogene (Chr22.4) variable region (subgroup V kappa II)
2.47	Hs.302046 Homo sapiens mRNA; cDNA DKFZp564C163 (from clone DKFZp564C163)
2.46	Hs.54517 ficolin (collagenfibrinogen domain-containing lectin) 2 (hucolin)
2.44	Hs.79706 plectin 1, intermediate filament binding protein, 500kD
2.44	Hs.274509 T cell receptor gamma constant 2
2.44	Hs.192662 hypothetical protein FLJ10469
2.42	Hs.81182 histamine N-methyltransferase
2.41	Hs.272034 hypothetical protein PRO2822
2.39	Hs.112259 T cell receptor gamma locus
2.38	gb:BC006252.1 /DEF=Homo sapiens, clone MGC:10619, mRNA, complete cds.
2.38	Hs.307187 H.sapiens mRNA for soluble delta TCR
2.37	Hs.283640 clg01 protein
2.37	Hs.196352 neutrophil cytosolic factor 4 (40kD)
2.37	Hs.143212 cystatin F (leukocystatin)
2.36	Hs.211869 dickkopf (Xenopus laevis) homolog 2
2.34	Hs.105700 secreted frizzled-related protein 4
2.34	Hs.183805 ankyrin 1, erythrocytic
2.34	Hs.78909 butyrate response factor 2 (EGF-response factor 2)
2.34	Hs.150443 KIAA0320 protein
2.33	Hs.171921 sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3C
2.33	Hs.287372 V1R-like 1
2.32	Hs.2014 T cell receptor delta locus
2.30	gb:M18728.1 /DEF=Human nonspecific crossreacting antigen mRNA, complete cds.
2.30	Hs.287778 Human DNA sequence from clone RP11-318P23 on chromosome 20 Contains a TAR DNA-binding protein pseudogene, ESTs, STSs and GSSs
2.29	Hs.16611 tumor protein D52-like 1
2.29	Hs.195464 filamin A, alpha (actin-binding protein-280)
2.26	Hs.3066 granzyme K (serine protease, granzyme 3; tryptase II)
2.26	Hs.169824 killer cell lectin-like receptor subfamily B, member 1
2.25	Hs.171596 EphA2
2.25	Hs.81988 disabled (Drosophila) homolog 2 (mitogen-responsive phosphoprotein)
2.24	Hs.149255 phosphatidylinositol-4-phosphate 5-kinase, type I, alpha
2.24	Hs.306664 Homo sapiens cDNA FLJ14061 fis, clone HEMBB1000749
2.23	Hs.80731 autocrine motility factor receptor
2.23	Hs.74085 DNA segment on chromosome 12 (unique) 2489 expressed sequence
2.23	Hs.301289 Homo sapiens cDNA FLJ12427 fis, clone MAMMA1003127, highly similar to MYOSIN I ALPHA
2.22	Hs.272209 Homo sapiens cDNA FLJ10133 fis, clone HEMBA1003067
2.21	Hs.112259 T cell receptor gamma locus
2.21	Hs.195464 filamin A, alpha (actin-binding protein-280)
2.19	Hs.83169 matrix metalloproteinase 1 (interstitial collagenase)
2.19	Hs.93728 pre-B-cell leukemia transcription factor 2
2.18	Hs.98428 homeo box B6
2.18	Hs.143897 dysferlin, limb girdle muscular dystrophy 2B (autosomal recessive)
2.17	Hs.7647 MYC-associated zinc finger protein (purine-binding transcription factor)
2.17	Hs.2200 perforin 1 (pore forming protein)
2.16	Hs.78944 regulator of G-protein signalling 2, 24kD
2.16	Hs.183805 ankyrin 1, erythrocytic
2.16	Hs.75909 KIAA0182 protein
2.16	Hs.287621 hypothetical protein FLJ14069
2.15	Hs.112360 prominin (mouse)-like 1
2.15	Hs.169266 neuropeptide Y receptor Y1
2.15	Hs.118796 annexin A6
2.15	Hs.195464 filamin A, alpha (actin-binding protein-280)
2.14	Hs.50964 carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)
2.13	Hs.183805 ankyrin 1, erythrocytic
2.10	Hs.553 solute carrier family 6 (neurotransmitter transporter, serotonin), member 4

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

2.09	Hs.2463 angiopoietin 1
2.09	Hs.1724 interleukin 2 receptor, alpha
2.09	Hs.306667 Homo sapiens cDNA FLJ14076 fis, clone HEMBB1001925
2.07	Hs.308026 major histocompatibility complex, class II, DR beta 5
2.07	Hs.107526 UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 5
2.05	intersectin 1 (SH3 domain protein)
2.04	Hs.143288 hypothetical protein MGC11271
2.04	Hs.45743 adenosine A2b receptor
2.04	Hs.2014 T cell receptor delta locus
2.04	Hs.192657 NPHS2 gene (podocin)
2.03	Hs.75106 clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2, testosterone-repressed prostate message 2, apolipoprotein J)
2.02	Hs.814 major histocompatibility complex, class II, DP beta 1
2.02	Hs.160483 erythrocyte membrane protein band 7.2 (stomatin)
2.02	Hs.50477 RAB27A, member RAS oncogene family
2.00	Hs.288983 hypothetical protein FLJ21477
2.00	Hs.272391 taste receptor, type 2, member 9
1.98	Hs.858 v-rel avian reticuloendotheliosis viral oncogene homolog B (nuclear factor of kappa light polypeptide gene enhancer in B-cells 3)
1.97	Hs.6641 kinesin family member 5C
1.97	Hs.51305 v-maf musculoaponeurotic fibrosarcoma (avian) oncogene family, protein F
1.96	Hs.7718 hypothetical protein FLJ22678
1.96	Hs.2631 desmoglein 2
1.95	Hs.197114 RNA binding protein; AT-rich element binding factor
1.94	Hs.286079 spinocerebellar ataxia 8
1.94	Hs.13684 hypothetical protein FLJ10761
1.93	Hs.79077 KIAA0233 gene product
1.92	Hs.88411 lymphocyte antigen 117
1.91	Hs.77886 lamin AC
1.91	Hs.116550 ESTs
1.90	Hs.168669 oxoglutarate dehydrogenase (lipoamide)
1.89	Hs.2551 adrenergic, beta-2-, receptor, surface
1.89	Hs.73239 hypothetical protein FLJ10901
1.88	Hs.169222 acrosomal vesicle protein 1
1.88	Hs.69319 CA11
1.87	Hs.79601 /len=613
1.87	Hs.183805 ankyrin 1, erythrocytic
1.87	gb:BC005851.1 /DEF=Homo sapiens, Rho GDP dissociation inhibitor (GDI) alpha, clone MGC:2810, mRNA, complete cds.
1.87	Hs.121555 myosin IE
1.87	Hs.24048 FK506 binding protein precursor
1.86	Hs.195850 keratin 5 (epidermolysis bullosa simplex, Dowling-MearaKobnerWeber-Cockayne types)
1.86	Hs.115246 mutS (E. coli) homolog 4
1.86	Hs.41143 phosphoinositide-specific phospholipase C-beta 1
1.85	Hs.181002 MLL septin-like fusion
1.85	gb:NM_031286.1 /DEF=Homo sapiens SH3BGRL3-like protein (SH3BGRL3), mRNA.
1.84	KIAA0620 protein
1.84	Hs.32168 KIAA0442 protein
1.84	Hs.287534 hypothetical protein FLJ12568
1.83	Hs.139033 paternally expressed 3
1.83	Hs.75725 transgelin 2
1.83	Hs.8257 cytokine inducible SH2-containing protein
1.82	Hs.286049 phosphoserine aminotransferase
1.82	Hs.274150 hypothetical protein FLJ10351
1.81	Hs.289082 GM2 ganglioside activator protein
1.81	Hs.785 integrin, alpha 2b (platelet glycoprotein IIb of IIb/IIIa complex, antigen CD41B)
1.80	Hs.160483 erythrocyte membrane protein band 7.2 (stomatin)
1.80	Hs.50477 RAB27A, member RAS oncogene family
1.79	Hs.306531 Homo sapiens caspase-10c mRNA, complete cds

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

1.79	Hs.110915 interleukin 22 receptor
1.79	Hs.127561 myosin XV
1.79	Hs.211584 neurofilament, light polypeptide (68kD)
1.78	Hs.155191 villin 2 (ezrin)
1.78	Hs.241570 tumor necrosis factor (TNF superfamily, member 2)
1.78	Hs.304962 solute carrier family 4, sodium bicarbonate cotransporter-like, member 10
1.78	Hs.91299 guanine nucleotide binding protein (G protein), beta polypeptide 2
1.78	Hs.278295 cholinergic receptor, nicotinic, epsilon polypeptide
1.78	Hs.167529 cytochrome P450, subfamily IIC (mephenytoin 4-hydroxylase), polypeptide 9
1.77	Hs.102119 opsin 1 (cone pigments), short-wave-sensitive (color blindness, tritan)
1.76	dystrophia myotonica-containing WD repeat motif
1.76	Hs.57749 synaptic nuclei expressed gene 2; KIAA1011 protein
1.76	Hs.99491 RAS guanyl releasing protein 2 (calcium and DAG-regulated)
1.76	Hs.296348 E2k
1.75	Hs.176663 Fc fragment of IgG, low affinity IIIb, receptor for (CD16)
1.75	Hs.93837 phosphatidylinositol transfer protein, membrane-associated
1.75	Hs.81256 S100 calcium-binding protein A4 (calcium protein, calvasculin, metastasin, murine placental homolog)
1.75	Hs.11801 interferon regulatory factor 6
1.75	Hs.214982 laminin, gamma 1 (formerly LAMB2)
1.75	Hs.234799 breakpoint cluster region
1.75	Hs.97672 CTAGE-1 protein
1.74	Hs.195175 CASP8 and FADD-like apoptosis regulator
1.73	aquaporin 3
1.73	Hs.10247 activated leucocyte cell adhesion molecule
1.73	Hs.77910 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1 (soluble)
1.73	Hs.44 pleiotrophin (heparin binding growth factor 8, neurite growth-promoting factor 1)
1.73	Hs.195175 CASP8 and FADD-like apoptosis regulator
1.72	Hs.80645 interferon regulatory factor 1
1.72	Hs.77422 proteolipid protein 2 (colonic epithelium-enriched)
1.71	Hs.250696 KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3
1.71	Hs.44077 alpha-parvin
1.70	Hs.1103 transforming growth factor, beta 1
1.70	Hs.159161 Rho GDP dissociation inhibitor (GDI) alpha
1.70	Hs.153028 cytochrome b-561
1.70	Hs.279562 myelin transcription factor 1

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

DOWN REGULATED IN FUGETAXIS COMPARED TO CHEMOKINESIS SDF-1 GRADIENTS

-11.90	Hs.76364 allograft inflammatory factor 1
-9.57	Hs.15075 hypothetical protein DKFZp434E2216
-8.17	Hs.740 PTK2 protein tyrosine kinase 2
-7.80	Hs.78409 collagen, type XVIII, alpha 1
-6.94	Hs.156115 potassium voltage-gated channel, KQT-like subfamily, member 1
-6.69	Hs.85752 uncharacterized hematopoietic stemprogenitor cells protein MDS026
-6.20	Hs.82979 mitogen-activating protein kinase kinase kinase kinase 2
-6.13	Hs.74047 electron-transfer-flavoprotein, beta polypeptide
-6.13	Hs.14142 nudix (nucleoside diphosphate linked moiety X)-type motif 2
-6.00	Hs.78146 plateletendothelial cell adhesion molecule (CD31 antigen)
-5.85	Hs.283404 organic cation transporter
-5.76	Hs.76845 phosphoserine phosphatase-like
-5.54	Hs.82985 collagen, type V, alpha 2
-5.45	gb:M24668.1 /DEF=Human Ig rearranged H-chain V-region mRNA (C-D-JH4), complete cds.
-5.33	Hs.3743 matrix metalloproteinase 24 (membrane-inserted)
-5.30	Hs.165662 KIAA0675 gene product
-5.29	Hs.76591 KIAA0887 protein
-4.87	Hs.2399 matrix metalloproteinase 14 (membrane-inserted)
-4.86	Hs.58435 FYN-binding protein (FYB-120130)
-4.83	Hs.93597 cyclin-dependent kinase 5, regulatory subunit 1 (p35)
-4.59	Hs.226581 COX15 (yeast) homolog, cytochrome c oxidase assembly protein
-4.47	Hs.121102 vanin 2
-4.41	Hs.315478 Homo sapiens, Similar to pericentriolar material 1, clone MGC:8458, mRNA, complete cds
-4.39	Hs.25477 hypothetical protein FLJ21044 similar to Rbig1
-4.36	Hs.306781 Homo sapiens cDNA: FLJ21535 fis, clone COL06131
-4.29	Hs.22370 Homo sapiens mRNA; cDNA DKFZp564O0122 (from clone DKFZp564O0122)
-4.26	Hs.168737 ESTs, Highly similar to 2AAB_HUMAN SERINETHREONINE PROTEIN PHOSPHATASE 2A, 65 KDA REGULATORY SUBUNIT A, BETA ISOFORM H.sapiens
-4.25	Hs.287912 lectin, mannose-binding, 1
-4.16	Hs.158241 KIAA0507 protein
-4.13	Hs.293334 ESTs
-4.11	Hs.24322 ATPase, H+ transporting, lysosomal (vacuolar proton pump) 9kD
-4.05	Hs.99987 excision repair cross-complementing rodent repair deficiency, complementation group 2 (xeroderma pigmentosum D)
-4.02	Hs.11135 major histocompatibility complex, class II, DN alpha
-3.99	Hs.41693 DnaJ (Hsp40) homolog, subfamily B, member 4
-3.98	Hs.73172 growth factor independent 1
-3.97	Hs.203269 ESTs, Moderately similar to ALU8_HUMAN ALU SUBFAMILY SX SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens
-3.95	Hs.197335 plasma glutamate carboxypeptidase
-3.93	gb:M24669.1 /DEF=Human Ig rearranged H-chain V-region mRNA (C-D-JH6), complete cds.
-3.92	Hs.296745 Homo sapiens cDNA FLJ13833 fis, clone THYRO1000676
-3.91	Hs.112751 KIAA0892 protein
-3.88	Hs.332381 hypothetical protein MGC4645
-3.75	Hs.225939 sialyltransferase 9 (CMP-NeuAc:lactosylceramide alpha-2,3-sialyltransferase; GM3 synthase)
-3.72	Hs.180686 ubiquitin protein ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome)
-3.70	Hs.264 GS2 gene
-3.68	Hs.48269 vaccinia related kinase 1
-3.68	Hs.1975 hypothetical protein FLJ21007
-3.64	Hs.209646 KIAA1118 protein
-3.63	Hs.11127 PET112 (yeast homolog)-like
-3.60	Hs.44865 lymphoid enhancer binding factor-1
-3.59	Hs.296821 Human facioscapulohumeral muscular dystrophy (FSHD) gene region, D4Z4 tandem repeat unit
-3.55	Hs.5378 spondin 1, (f-spondin) extracellular matrix protein
-3.53	Hs.117242 meningioma expressed antigen 6 (coiled-coil proline-rich)
-3.52	Hs.106650 hypothetical protein FLJ20533

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

-3.50	Hs.279862 cdk inhibitor p21 binding protein
-3.48	Hs.8173 hypothetical protein FLJ10803
-3.46	Hs.86178 M-phase phosphoprotein 9
-3.44	Hs.20894 N-deacetylaseN-sulfotransferase (heparan glucosaminyl) 1
-3.44	Hs.168586 NCX protein
-3.44	Hs.73980 troponin T1, skeletal, slow
-3.43	Hs.237323 N-acetylglucosamine-phosphate mutase
-3.43	Hs.132560 hypothetical protein FLJ10312
-3.42	gb:NM_030895.1 /DEF=Homo sapiens hypothetical protein FLJ14129 (FLJ14129), mRNA.
-3.41	Hs.89560 iduronidase, alpha-L-
-3.37	Hs.184019 Homo sapiens clone 23551 mRNA sequence
-3.37	Hs.121128 BCR downstream signaling 1
-3.32	Hs.262869 plasminogen-like
-3.29	Hs.129218 KIAA1074 protein
-3.29	Hs.47344 advillin
-3.24	Hs.223014 antizyme inhibitor
-3.17	Hs.78518 natriuretic peptide receptor Bguanylate cyclase B (atrionatriuretic peptide receptor B)
-3.17	Hs.158688 KIAA0741 gene product
-3.17	Hs.20137 hypothetical protein DKFZp434P0116
-3.15	Hs.155049 hypothetical protein FLJ11282
-3.15	Hs.120769 Homo sapiens cDNA FLJ20463 fis, clone KAT06143
-3.13	Hs.173594 serine (or cysteine) proteinase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 1
-3.12	Hs.7426 KIAA0841 protein
-3.11	Hs.61712 pyruvate dehydrogenase kinase, isoenzyme 1
-3.11	Hs.110796 SAR1 protein
-3.11	Hs.105478 phosphoribosylformylglycinamidine synthase (FGAR amidotransferase)
-3.10	Hs.14286 flavin containing monooxygenase 5
-3.08	Hs.61289 synaptojanin 2
-3.06	Hs.23796 odz (odd Ozten-m, Drosophila) homolog 1
-3.04	Hs.249216 H2B histone family, member J
-3.03	Hs.6179 DEADH (Asp-Glu-Ala-AspHis) box polypeptide 17 (72kD)
-3.03	Hs.104916 hypothetical protein FLJ21940
-3.03	Hs.184523 KIAA0965 protein
-3.03	Hs.175038 HSPC056 protein
-3.02	Hs.314534 ESTs, Moderately similar to ALU5_HUMAN ALU SUBFAMILY SC SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens
-3.01	Hs.9192 Homer, neuronal immediate early gene, 1B
-2.99	Hs.296371 RAB28, member RAS oncogene family
-2.99	Hs.49994 Homo sapiens, clone MGC:10871, mRNA, complete cds
-2.98	Hs.305960 hemoglobin, gamma A
-2.97	Hs.29189 ATPase, Class VI, type 11A
-2.94	Hs.109526 zinc finger protein 198
-2.94	Hs.287763 Human DNA sequence from clone RP1-23O21 on chromosome 6. Contains an acidic calponin 3 (CNN3) pseudogene, STSs and GSSs
-2.93	Hs.279803 hypothetical protein DKFZp566H0824
-2.93	Hs.26899 KIAA0285 gene product
-2.93	Hs.325530 KIAA1067 protein
-2.92	Hs.227280 U6 snRNA-associated Sm-like protein
-2.92	Hs.129928 KIAA0477 gene product
-2.91	Hs.79993 peroxisomal biogenesis factor 7
-2.90	Hs.109655 sex comb on midleg (Drosophila)-like 1
-2.89	Hs.13501 pescadillo (zebrafish) homolog 1, containing BRCT domain
-2.89	Hs.86178 M-phase phosphoprotein 9
-2.88	Hs.79170 KIAA0227 protein
-2.86	Hs.42331 ephrin-A4
-2.86	Hs.44697 ATPase, Class V, type 10C
-2.84	Hs.18069 protease, cysteine, 1 (legumain)
-2.84	Hs.211933 collagen, type XIII, alpha 1

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

-2.82	Hs.20019 hemochromatosis
-2.81	Human DNA sequence from clone RP5-1163J1 on chromosome 22q13.2-13.33 Contains the 3' part of a gene for a novel KIAA0279 LIKE EGF-like domain containing protein (similar to mouse Celsr1, rat MEGF2), a novel gene for a protein similar to C. elegans B0035.1
-2.81	Hs.221040 HBS1 (S. cerevisiae)-like
-2.80	Hs.292998 ESTs
-2.79	Hs.38783 SKI-like
-2.79	Hs.168625 androgen-induced prostate proliferative shutoff associated protein
-2.78	Hs.174185 ectonucleotide pyrophosphatasephosphodiesterase 2 (autotaxin)
-2.77	Hs.1460 glucagon
-2.77	Hs.23585 KIAA1078 protein
-2.75	Hs.5241 fatty acid binding protein 1, liver
-2.75	Hs.82527 sialyltransferase 8 (alpha-N-acetylneuraminate: alpha-2,8-sialytransferase, GD3 synthase) A
-2.75	Hs.31476 Homo sapiens cDNA FLJ13872 fis, clone THYRO1001322
-2.72	Hs.18858 phospholipase A2, group IVC (cytosolic, calcium-independent)
-2.69	KIAA1117 protein
-2.69	Hs.26471 Homo sapiens clone HQ0692
-2.69	Hs.239114 mannosidase, alpha, class 1A, member 2
-2.68	Hs.226213 cytochrome P450, 51 (lanosterol 14-alpha-demethylase)
-2.68	Hs.262869 plasminogen-like
-2.68	gb:BC006356.1 /DEF=Homo sapiens, NCX protein, clone MGC:12870, mRNA, complete cds.
-2.68	Hs.106823 H.sapiens gene from PAC 426I6, similar to syntaxin 7
-2.68	Hs.294014 ESTs
-2.65	Hs.75574 mitochondrial ribosomal protein L19
-2.65	Hs.168640 ankylosis, progressive (mouse) homolog
-2.64	Hs.241493 natural killer-tumor recognition sequence
-2.62	Hs.100014 glutamate receptor, ionotrophic, AMPA 3
-2.62	Hs.2864 early endosome antigen 1, 162kD
-2.62	Hs.79368 epithelial membrane protein 1
-2.60	Hs.13980 ubiquitously transcribed tetratricopeptide repeat gene, X chromosome
-2.60	Hs.28777 H2A histone family, member L
-2.60	Hs.274131 Down syndrome critical region gene 1-like 2
-2.58	Hs.170307 Ral guanine nucleotide exchange factor RalGPS1A
-2.58	Hs.94037 hypothetical protein FLJ23053
-2.58	Hs.295923 seven in absentia (Drosophila) homolog 1
-2.57	Hs.46821 hypothetical protein FLJ20086
-2.56	Hs.144563 tryptophan hydroxylase (tryptophan 5-monooxygenase)
-2.56	Hs.35091 hypothetical protein FLJ10775
-2.55	Hs.288931 Homo sapiens cDNA FLJ13034 fis, clone NT2RP3001232
-2.55	Hs.171545 HIV-1 Rev binding protein
-2.53	Hs.59594 /len=529
-2.53	Hs.194669 enhancer of zeste (Drosophila) homolog 1
-2.53	Hs.151010 ESTs
-2.52	Hs.6700 /len=604
-2.51	Hs.207805 Homo sapiens mRNA; cDNA DKFZp564I066 (from clone DKFZp564I066)
-2.49	Hs.165662 KIAA0675 gene product
-2.49	Hs.183291 zinc finger protein 268
-2.49	Hs.73742 ribosomal protein, large, P0
-2.49	Hs.12533 Homo sapiens clone 23705 mRNA sequence
-2.49	Hs.271926 serologically defined colon cancer antigen 16
-2.48	Hs.74624 protein tyrosine phosphatase, receptor type, N polypeptide 2
-2.48	Hs.222306 hypothetical protein MGC3329
-2.47	Hs.966 coilin
-2.47	Hs.158205 basic leucine zipper nuclear factor 1 (JEM-1)
-2.45	Hs.271699 polymerase (DNA directed) iota
-2.44	Hs.5131 hypothetical protein FLJ20654
-2.43	Hs.237849 ESTs
-2.42	Hs.32942 phosphoinositide-3-kinase, catalytic, gamma polypeptide

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

-2.42	Hs.40202 lymphoid-restricted membrane protein
-2.42	Hs.188710 ESTs
-2.38	Hs.17200 STAM-like protein containing SH3 and ITAM domains 2
-2.38	Hs.170279 tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)
-2.38	Hs.36972 CD7 antigen (p41)
-2.37	Hs.101299 cullin 5
-2.37	Hs.2558 bone gamma-carboxyglutamate (gla) protein (osteocalcin)
-2.37	Hs.272572 hemoglobin, alpha 2
-2.35	Hs.82919 cullin 2
-2.35	Hs.171558 sex comb on midleg (Drosophila)-like 2
-2.35	Hs.95907 multiple inositol polyphosphate phosphatase 1
-2.35	Hs.210431 Homo sapiens mRNA; cDNA DKFZp434N144 (from clone DKFZp434N144)
-2.34	Hs.11494 fibulin 5
-2.34	Hs.25155 neuroepithelial cell transforming gene 1
-2.34	Hs.78146 plateletendothelial cell adhesion molecule (CD31 antigen)
-2.34	Hs.23642 protein predicted by clone 23627
-2.34	Hs.278064 Homo sapiens cDNA: FLJ23327 fis, clone HEP12630, highly similar to HSZNF37 Homo sapiens ZNF37A mRNA for zinc finger protein
-2.33	Hs.5022 imprinted in Prader-Willi syndrome
-2.32	Hs.78946 cullin 3
-2.32	Hs.23240 Homo sapiens cDNA FLJ13496 fis, clone PLACE1004471, weakly similar to ZINC FINGER PROTEIN 83
-2.31	Hs.223241 eukaryotic translation elongation factor 1 delta (guanine nucleotide exchange protein)
-2.30	Hs.194148 v-yes-1 Yamaguchi sarcoma viral oncogene homolog 1
-2.30	gb:S82471.1 /DEF=Homo sapiens Kruppel-associated box containing gene product SSX3 (SSX3) mRNA, complete cds.
-2.30	Hs.86434 hypothetical protein FLJ21816
-2.28	Hs.175941 B-cell receptor-associated protein BAP29
-2.26	Hs.96264 alpha thalassemiamental retardation syndrome X-linked (RAD54 (S. cerevisiae) homolog)
-2.26	Hs.75231 solute carrier family 16 (monocarboxylic acid transporters), member 1
-2.26	Hs.69559 KIAA1096 protein
-2.25	Hs.23964 sin3-associated polypeptide, 18kD
-2.25	Hs.94376 proprotein convertase subtilisinkexin type 5
-2.25	Hs.62187 phosphatidylinositol glycan, class K
-2.25	Hs.272534 Homo sapiens mRNA; cDNA DKFZp564J062 (from clone DKFZp564J062)
-2.24	Hs.74861 activated RNA polymerase II transcription cofactor 4
-2.23	Hs.306602 Homo sapiens cDNA FLJ11514 fis, clone HEMBA1002229
-2.22	Hs.279777 hypothetical protein
-2.21	Hs.797 nuclear transcription factor Y, alpha
-2.19	Hs.77868 ORF
-2.18	Hs.102456 survival of motor neuron protein interacting protein 1
-2.18	Hs.234265 DKFZP586G011 protein
-2.17	Hs.117313 Meis (mouse) homolog 3
-2.16	Hs.155140 casein kinase 2, alpha 1 polypeptide
-2.15	gb:NM_031206.1 /DEF=Homo sapiens hypothetical protein FLJ12525 (FLJ12525), mRNA.
-2.15	Hs.100914 hypothetical protein FLJ10352
-2.14	Hs.15791 transmembrane 7 superfamily member 1 (upregulated in kidney)
-2.14	Hs.75694 mannose phosphate isomerase
-2.14	Hs.278985 hypothetical protein
-2.14	Hs.142570 Homo sapiens clone 24629 mRNA sequence
-2.14	Hs.247904 Human DNA sequence from clone 1060K6 on chromosome 20p12.1-13 Contains a pseudogene similar to 40S ribosomal protein S11, ESTs, STSs and GSSs
-2.13	Hs.237146 hypothetical protein FLJ12752
-2.12	Hs.279902 cofactor required for Sp1 transcriptional activation, subunit 9 (33kD)
-2.12	Hs.57553 tousled-like kinase 2
-2.11	Hs.166733 leucylcystinyl aminopeptidase
-2.11	Hs.114408 toll-like receptor 5
-2.10	Hs.119023 SMC2 (structural maintenance of chromosomes 2, yeast)-like 1
-2.10	Hs.22182 zinc finger protein 23 (KOX 16)

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

-2.08	Hs.2815 POU domain, class 6, transcription factor 1
-2.08	Hs.82065 interleukin 6 signal transducer (gp130, oncostatin M receptor)
-2.07	gb:AF356353.1 /DEF=Homo sapiens spindlin-like protein 2 (SPIN2) mRNA, complete cds.
-2.06	Hs.306613 Homo sapiens cDNA FLJ11740 fis, clone HEMBA1005500
-2.06	Hs.105633 hypothetical protein FLJ10583
-2.05	Hs.82143 E74-like factor 2 (ets domain transcription factor)
-2.05	Hs.43549 uncharacterized hematopoietic stemprogenitor cells protein MDS029
-2.04	Hs.283709 lipopolysaccharide specific response-7 protein
-2.03	Hs.126908 hypothetical protein FLJ12994
-2.03	Hs.5997 hypothetical protein FLJ13078
-2.02	Hs.202695 Human soluble CD44 (CD44) mRNA, with exon v9 extension, partial cds
-2.02	Hs.42785 DC11 protein
-2.02	gb:NM_031268.1 /DEF=Homo sapiens PRO0461 protein (PRO0461), mRNA.
-2.01	Hs.300741 sorcin
-2.01	Hs.91165 hypothetical protein
-2.00	Hs.24485 chondroitin sulfate proteoglycan 6 (bamacan)
-2.00	Hs.311 phosphoribosyl pyrophosphate amidotransferase
-2.00	Hs.296290 Homo sapiens cDNA FLJ13357 fis, clone PLACE1000061, weakly similar to Human ribosomal protein L37a mRNA sequence
-1.99	Hs.251577 hemoglobin, alpha 1
-1.99	Hs.99847 peroxisome biogenesis factor 1
-1.99	Hs.7194 CGI-74 protein
-1.98	Hs.39328 /len=463
-1.98	Hs.96063 insulin receptor substrate 1
-1.98	Hs.93391 hypothetical protein FLJ10539
-1.98	Hs.48950 heptacellular carcinoma novel gene-3 protein
-1.97	Hs.13225 UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 4
-1.96	Hs.234757 Human lipocortin (LIP) 2 pseudogene mRNA, complete cds-like region
-1.96	Hs.302114 Human DNA sequence from clone RP5-843L14 on chromosome 20. Contains ESTs, STSs and GSSs. Contains a novel gene and the 5 part of a gene for a novel protein similar to X-linked ribosomal protein 4 (RPS4X)
-1.96	Hs.283753 cell cycle progression 8 protein
-1.95	Hs.184050 v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene homolog
-1.95	Hs.2074 zinc finger protein, X-linked
-1.95	Hs.135202 c-myc promoter-binding protein
-1.94	Hs.3530 TLS-associated serine-arginine protein 2
-1.94	Hs.97681 DNA (cytosine-5-)-methyltransferase 2
-1.94	Hs.12835 A kinase (PRKA) anchor protein 7
-1.94	Hs.1592 CDC16 (cell division cycle 16, S. cerevisiae, homolog)
-1.94	Hs.325520 Homo sapiens IMAA mRNA for hLAT1-3TM, complete cds
-1.94	Hs.20447 protein kinase related to S. cerevisiae STE20, effector for Cdc42Hs
-1.93	Hs.155995 KIAA0643 protein
-1.91	Hs.4310 eukaryotic translation initiation factor 1A
-1.91	Hs.20952 Homo sapiens clone 24411 mRNA sequence
-1.91	Hs.16951 DKFZP586P2219 protein
-1.90	Hs.158205 basic leucine zipper nuclear factor 1 (JEM-1)
-1.90	Hs.14968 pleiomorphic adenoma gene 1
-1.90	Hs.33363 DKFZP434N093 protein
-1.89	Hs.300684 calcitonin gene-related peptide-receptor component protein
-1.89	Hs.265561 CD2-associated protein
-1.89	Hs.81452 fatty-acid-Coenzyme A ligase, long-chain 4
-1.89	Hs.109526 zinc finger protein 198
-1.89	Hs.179507 KIAA0779 protein
-1.87	Hs.16079 hypothetical protein FLJ10233
-1.86	Hs.11899 3-hydroxy-3-methylglutaryl-Coenzyme A reductase
-1.86	Hs.158195 heat shock transcription factor 2
-1.86	Hs.124126 Homo sapiens clone 24438 mRNA sequence
-1.86	Hs.287391 Homo sapiens chromosome 19, cosmid F23269
-1.85	Hs.288986 survival of motor neuron 1, telomeric

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

-1.85	Hs.54697 Cdc42 guanine exchange factor (GEF) 9
-1.85	Hs.239106 solute carrier family 3 (cystine, dibasic and neutral amino acid transporters, activator of cystine, dibasic and neutral amino acid transport), member 1
-1.84	Hs.117852 ATP-binding cassette, sub-family D (ALD), member 2
-1.84	Hs.301114 zinc finger protein 79 (pT7)
-1.84	Hs.285107 hypothetical protein FLJ13397
-1.84	Hs.50579 hypothetical protein FLJ20718
-1.84	Hs.44856 hypothetical protein FLJ12116
-1.84	Hs.279932 CGI-105 protein
-1.84	Hs.293495 ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens
-1.83	Hs.9884 spindle pole body protein
-1.83	Hs.170198 KIAA0009 gene product
-1.83	Hs.111244 hypothetical protein
-1.83	Hs.75692 asparagine synthetase
-1.83	Hs.72160 AND-1 protein
-1.83	Hs.324275 Homo sapiens mRNA; cDNA DKFZp434D2111 (from clone DKFZp434D2111)
-1.83	Hs.126779 KIAA0752 protein
-1.81	Hs.184245 KIAA0929 protein Msx2 interacting nuclear target (MINT) homolog
-1.81	Hs.118174 tetratricopeptide repeat domain 3
-1.81	Hs.29131 nuclear receptor coactivator 2
-1.81	Hs.22559 KIAA0197 protein
-1.81	Hs.136644 CS box-containing WD protein
-1.80	Hs.174795 PDZ domain-containing guanine nucleotide exchange factor I
-1.79	Hs.122607 B-cell CLLlymphoma 9
-1.79	Hs.78935 methionine aminopeptidase; eIF-2-associated p67
-1.79	Hs.43946 L13 protein
-1.78	Hs.1540 nuclear matrix protein p84
-1.78	Hs.8117 erbb2-interacting protein ERBIN
-1.78	Hs.279851 hypothetical protein FLJ10241
-1.78	Hs.82664 ETAA16 protein
-1.77	Hs.283609 hypothetical protein PRO2032
-1.77	Hs.279819 APR-1 protein
-1.76	Hs.118738 KIAA0800 gene product
-1.76	Hs.118978 KIAA0256 gene product
-1.76	Hs.111373 KIAA0423 protein
-1.76	Hs.22549 hypothetical protein FLJ12799
-1.75	Hs.78221 c-myc binding protein
-1.75	Hs.180324 YY1-associated factor 2
-1.75	Hs.240112 KIAA0276 protein
-1.75	Hs.325667 TMTSP for transmembrane molecule with thrombospondin module
-1.74	Hs.83715 Sjogren syndrome antigen B (autoantigen La)
-1.74	Hs.6241 phosphoinositide-3-kinase, regulatory subunit, polypeptide 1 (p85 alpha)
-1.74	Hs.127416 synaptojanin 1
-1.74	Hs.236642 3-hydroxyisobutyryl-Coenzyme A hydrolase
-1.74	Hs.301800 Homo sapiens cDNA FLJ11568 fis, clone HEMBA1003278
-1.74	Hs.247782 Human DNA sequence from clone 581F12 on chromosome Xq21. Contains Eukaryotic Translation Initiation Factor EIF3 P35 Subunit and 60S Ribosomal protein L22 pseudogenes. Contains ESTs
-1.74	Hs.30057 transporter similar to yeast MRS2
-1.73	Hs.79078 MAD2 (mitotic arrest deficient, yeast, homolog)-like 1
-1.73	Hs.180919 inhibitor of DNA binding 2, dominant negative helix-loop-helix protein
-1.73	Hs.154740 TBP-interacting protein
-1.73	Hs.247309 succinate-CoA ligase, GDP-forming, beta subunit
-1.72	Hs.180895 putative brain nuclearly-targeted protein
-1.72	Hs.84560 hypothetical protein FLJ11795
-1.72	Hs.249495 heterogeneous nuclear ribonucleoprotein A1
-1.71	Hs.75140 low density lipoprotein-related protein-associated protein 1 (alpha-2-macroglobulin receptor-associated protein 1)
-1.71	Hs.285848 KIAA1454 protein

FIGURE 6

Table 4
Differential Gene Expression in Chemokinesis vs Fugetaxis SDF-1 Gradients

-1.71	Hs.8198 zinc finger protein 204
-1.71	Hs.7432 hypothetical protein FLJ10477
-1.71	Hs.301406 hypothetical protein PP3501
-1.70	Hs.286027 etoposide-induced mRNA
-1.70	Hs.293219 ESTs

FIGURE 7

Table 5
Differential Gene Expression in Medium vs Chemotaxis SDF-1 Gradients

UP REGULATED IN CHEMOTAXIS COMPARED TO MEDIUM SDF-1 GRADIENTS

78.70	Hs.80358 SMC (mouse) homolog, Y chromosome
71.90	Hs.99120 DEADH (Asp-Glu-Ala-AspHis) box polypeptide, Y chromosome
54.36	Hs.180911 ribosomal protein S4, Y-linked
29.71	Hs.193145 ubiquitin specific protease 9, Y chromosome (Drosophila fat facets related)
22.20	Hs.155103 eukaryotic translation initiation factor 1A, Y chromosome
18.91	Hs.155397 Homo sapiens mRNA; cDNA DKFZp564K143 (from clone DKFZp564K143)
16.39	Hs.73931 major histocompatibility complex, class II, DQ beta 1
14.73	Hs.99120 DEADH (Asp-Glu-Ala-AspHis) box polypeptide, Y chromosome
13.49	Hs.177605 killer cell lectin-like receptor subfamily C, member 2
12.83	Hs.73931 major histocompatibility complex, class II, DQ beta 1
10.71	Hs.155103 eukaryotic translation initiation factor 1A, Y chromosome
9.06	Hs.301636 peroxisomal biogenesis factor 6
7.34	Hs.2014 T cell receptor delta locus
6.76	Hs.3195 small inducible cytokine subfamily C, member 1 (lymphotactin)
6.19	Hs.326035 early growth response 1
6.08	Hs.56336 protein kinase, Y-linked
5.43	Hs.194689 artemin
5.04	gb:BC005921.1 /DEF=Homo sapiens, chorionic somatomammotropin hormone 1 (placental lactogen), clone MGC:14518, mRNA, complete cds.
4.77	Hs.194746 calcium channel, voltage-dependent, alpha 1G subunit
4.73	Hs.279953 EH domain-binding mitotic phosphoprotein
4.53	gb:M32577.1 /DEF=Human MHC HLA-DQ beta mRNA, complete cds.
4.46	Hs.6891 splicing factor, arginineserine-rich 6
3.99	Hs.187617 hypothetical protein FLJ13941
3.95	Hs.98614 ribosome binding protein 1 (dog 180kD homolog)
3.59	Hs.288915 Homo sapiens cDNA FLJ12346 fis, clone MAMMA1002297, highly similar to Homo sapiens mRNA for Rab6 GTPase activating protein
3.56	Hs.1447 glial fibrillary acidic protein
3.50	Hs.279891 truncated calcium binding protein
3.45	Hs.307105 Human DNA sequence from clone RP11-278J20 on chromosome 6. Contains ESTs, STSs and GSSs. Contains an RBBP4 (retinoblastoma-binding protein 4) pseudogene and a KIAA0797 pseudogene
3.42	Hs.211280 ESTs, Weakly similar to WN7A_HUMAN WNT-7A PROTEIN PRECURSOR H.sapiens
3.36	Hs.184915 zinc finger protein, Y-linked
3.33	Hs.79706 plectin 1, intermediate filament binding protein, 500kD
3.31	Hs.2352 adenylate cyclase 2 (brain)
3.30	Hs.79019 baculoviral IAP repeat-containing 1
3.16	Hs.75842 dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 1A
3.10	Hs.6363 heparan sulfate 6-O-sulfotransferase
3.06	Hs.307187 H.sapiens mRNA for soluble delta TCR
3.05	Hs.73742 ribosomal protein, large, P0
3.04	Hs.73078 deleted in azoospermia-like
2.96	Hs.306425 Homo sapiens mRNA for KIAA1417 protein, partial cds
2.95	Hs.249216 H2B histone family, member J
2.91	Hs.36972 CD7 antigen (p41)
2.90	Hs.91103 Homo sapiens, Similar to CG2245 gene product, clone MGC:4293, mRNA, complete cds
2.87	Hs.274230 3-phosphoadenosine 5-phosphosulfate synthase 2
2.85	Hs.46332 G protein-coupled receptor 6
2.71	gb:NM_030773.1 /DEF=Homo sapiens beta tubulin 1, class VI (TUBB1), mRNA.
2.71	Hs.21486 signal transducer and activator of transcription 1, 91kD
2.64	Hs.103978 serinethreonine kinase 22B (spermiogenesis associated)
2.59	Hs.164960 BarH-like homeobox 1
2.58	Hs.82503 H.sapiens mRNA for 3UTR of unknown protein
2.57	Hs.319088 hypothetical protein FLJ10375
2.55	Hs.184915 zinc finger protein, Y-linked
2.49	Hs.37040 platelet-derived growth factor alpha polypeptide
2.44	Hs.23965 solute carrier family 22 (organic anion transporter), member 6
2.41	Hs.306618 Homo sapiens cDNA FLJ11930 fis, clone HEMBB1000441

FIGURE 7

Table 5
Differential Gene Expression in Medium vs Chemotaxis SDF-1 Gradients

2.40	Hs.272268 Human DNA sequence from clone RP1-18C9 on chromosome 20 Contains part of a novel gene similar to acetyl-coenzyme A synthetase, a novel gene (locus D20S101) similar to Gamma-glutamyltranspeptidase (contains CCA trinucleotide repeat), a gene simil
2.39	Hs.2014 T cell receptor delta locus
2.35	Hs.293205 ESTs, Weakly similar to BC39498 1 H.sapiens
2.34	Hs.55481 zinc finger protein 165
2.31	Hs.122764 BRCA1 associated protein
2.31	Hs.299567 G protein-coupled receptor 44
2.28	Hs.3838 serum-inducible kinase
2.25	Hs.79019 baculoviral IAP repeat-containing 1
2.25	gb:NM_030895.1 /DEF=Homo sapiens hypothetical protein FLJ14129 (FLJ14129), mRNA.
2.20	Hs.36972 CD7 antigen (p41)
2.20	Hs.306797 Homo sapiens cDNA: FLJ21648 fis, clone COL08469
2.19	Hs.8077 Homo sapiens mRNA; cDNA DKFZp547E184 (from clone DKFZp547E184)
2.16	Hs.753 formyl peptide receptor 1
2.09	Hs.280380 aminopeptidase
2.06	Hs.18586 KIAA0451 gene product
2.03	Hs.193606 Homo sapiens PAC clone RP5-1093O17 from 7q11.23-q21
1.99	Hs.146025 hypothetical protein FLJ23594
1.96	Hs.33862 ESTs
1.96	Hs.274402 heat shock 70kD protein 1B
1.94	Hs.75887 coatomer protein complex, subunit alpha
1.92	Hs.197805 SRY (sex determining region Y)-box 30
1.91	Hs.1521 immunoglobulin mu binding protein 2
1.90	Hs.15087 KIAA0250 gene product
1.88	Hs.167927 islet cell autoantigen 1 (69kD)
1.86	Hs.39733 postsynaptic protein CRIPT
1.85	Hs.76722 CCAATenhancer binding protein (CEBP), delta
1.84	Hs.265018 hypothetical protein FLJ20635
1.81	Hs.239737 C-terminal binding protein 1
1.80	Hs.33787 vinexin beta (SH3-containing adaptor molecule-1)
1.80	Hs.279582 GTP-binding protein Sara
1.80	Hs.324728 SMA5
1.79	Hs.44766 retinitis pigmentosa 2 (X-linked recessive)
1.77	Hs.288940 five-span transmembrane protein M83
1.74	Hs.247043 type 1 tumor necrosis factor receptor shedding aminopeptidase regulator
1.70	Hs.273099 Homo sapiens cDNA FLJ13712 fis, clone PLACE2000394

FIGURE 7

Table 5
Differential Gene Expression in Medium vs Chemotaxis SDF-1 Gradients

DOWN REGULATED IN CHEMOTAXIS COMPARED TO MEDIUM SDF-1 GRADIENTS

-10.88	Hs.51120 cathelicidin antimicrobial peptide
-10.70	Hs.73839 ribonuclease, RNase A family, 3 (eosinophil cationic protein)
-6.33	Hs.76845 phosphoserine phosphatase-like
-6.30	Hs.183362 hypothetical protein FLJ20535
-5.27	Hs.89535 bactericidalpermeability-increasing protein
-5.25	Hs.25477 hypothetical protein FLJ21044 similar to Rbig1
-5.18	Hs.26319 KIAA0833 protein
-4.78	Hs.153952 5 nucleotidase (CD73)
-4.51	Hs.4854 cyclin-dependent kinase inhibitor 2C (p18, inhibits CDK4)
-4.36	Hs.99863 elastase 2, neutrophil
-4.32	Hs.75498 small inducible cytokine subfamily A (Cys-Cys), member 20
-4.31	Hs.18889 DKFZP434M183 protein
-4.24	Hs.158278 KIAA0509 protein
-4.22	Hs.84673 troponin I, skeletal, slow
-4.14	Hs.159900 G protein-coupled receptor 15
-3.96	Hs.50748 chromosome 21 open reading frame 18
-3.89	Hs.306434 Homo sapiens mRNA for LST-1N protein
-3.86	Hs.109438 Homo sapiens clone 24775 mRNA sequence
-3.77	Hs.99960 membrane-spanning 4-domains, subfamily A, member 3 (hematopoietic cell-specific)
-3.73	Hs.248085 insulin upstream factor 1
-3.66	Hs.152251 frizzled (Drosophila) homolog 5
-3.62	Hs.248115 growth hormone secretagogue receptor
-3.55	Hs.2257 vitronectin (serum spreading factor, somatomedin B, complement S-protein)
-3.50	Hs.101915 Stargardt disease 3 (autosomal dominant)
-3.42	Hs.272795 hypothetical protein FLJ20359
-3.41	Hs.6164 hypothetical protein FLJ10698
-3.36	Hs.125783 DEME-6 protein
-3.32	Hs.278984 calcium binding protein 2
-3.29	Hs.154495 acetylcholinesterase (YT blood group)
-3.25	Hs.306763 Homo sapiens cDNA: FLJ21442 fis, clone COL04429, highly similar to HSA237839 Homo sapiens mRNA for hypothetical protein
-3.16	Hs.286124 CD24 antigen (small cell lung carcinoma cluster 4 antigen)
-3.13	Hs.1378 annexin A3
-3.10	Hs.949 neutrophil cytosolic factor 2 (65kD, chronic granulomatous disease, autosomal 2)
-3.10	Hs.18653 ESTs
-3.03	Hs.106070 cyclin-dependent kinase inhibitor 1C (p57, Kip2)
-2.96	Hs.111867 GLI-Kruppel family member GLI2
-2.95	Hs.20315 interferon-induced protein with tetratricopeptide repeats 1
-2.92	Hs.317169 hypothetical protein MGC10715
-2.89	Hs.26208 collagen, type XVI, alpha 1
-2.83	Hs.222153 ESTs, Moderately similar to archvillin H.sapiens
-2.78	Hs.226396 hypothetical protein FLJ11126
-2.73	Hs.58116 homeo box A2
-2.71	Hs.75608 tight junction protein 2 (zona occludens 2)
-2.69	Hs.21223 calponin 1, basic, smooth muscle
-2.69	Hs.251664 insulin-like growth factor 2 (somatomedin A)
-2.69	Hs.33084 solute carrier family 2 (facilitated glucose transporter), member 5
-2.60	Hs.241053 ESTs
-2.57	Hs.2582 defensin, alpha 4, corticostatin
-2.56	Hs.22972 hypothetical protein FLJ13352
-2.56	Hs.179747 ecotropic viral integration site 5
-2.52	Hs.133342 Homo sapiens clone 24566 mRNA sequence
-2.52	Hs.239737 C-terminal binding protein 1
-2.49	Hs.91971 cAMP-regulated guanine nucleotide exchange factor II
-2.48	Hs.9291 Homo sapiens cDNA FLJ13511 fis, clone PLACE1005331, highly similar to Homo sapiens 7h3 protein mRNA

FIGURE 7

Table 5
Differential Gene Expression in Medium vs Chemotaxis SDF-1 Gradients

-2.48	Hs.19520 FXYD domain-containing ion transport regulator 2
-2.47	Hs.77643 FK506-binding protein 1B (12.6 kD)
-2.45	Hs.193716 complement component (3b4b) receptor 1, including Knops blood group system
-2.45	Hs.296355 Homo sapiens cDNA: FLJ23138 fis, clone LNG08913
-2.45	Hs.19131 transcription factor Dp-2 (E2F dimerization partner 2)
-2.45	Hs.274463 defensin, alpha 1, myeloid-related sequence
-2.43	Hs.112049 SET binding factor 1
-2.43	Hs.283664 aspartate beta-hydroxylase
-2.42	Hs.121576 Homo sapiens cDNA FLJ20153 fis, clone COL08656, highly similar to AJ001381 Homo sapiens incomplete cDNA for a mutated allele
-2.37	Hs.287437 Homo sapiens cDNA FLJ11662 fis, clone HEMBA1004629
-2.35	Hs.21858 trinucleotide repeat containing 3
-2.35	Hs.23796 odz (odd Ozten-m, Drosophila) homolog 1
-2.33	Hs.282344 Homo sapiens cDNA FLJ13387 fis, clone PLACE1001136
-2.29	Hs.83623 nuclear receptor subfamily 1, group I, member 3
-2.29	Hs.31432 cardiac ankyrin repeat protein
-2.29	Hs.93758 H4 histone family, member H
-2.28	Hs.3781 similar to murine leucine-rich repeat protein
-2.24	Hs.41716 endothelial cell-specific molecule 1
-2.24	Hs.307353 Homo sapiens Chromosome 16 BAC clone CIT987SK-44M2
-2.22	Hs.292853 ESTs
-2.19	Hs.106552 cell recognition molecule Caspr2
-2.16	Hs.247910 Homo sapiens isolate donor N clone N88K immunoglobulin kappa light chain variable region mRNA, partial cds
-2.14	Hs.93597 cyclin-dependent kinase 5, regulatory subunit 1 (p35)
-2.07	Hs.283683 chromosome 8 open reading frame 4
-2.01	Hs.289056 ESTs, Highly similar to 1312232A kininogen L,high MW H.sapiens
-1.99	Hs.248190 UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 4 (GalNAc-T4)
-1.95	Hs.324730 glutathione S-transferase M1
-1.95	Hs.3628 mitogen-activated protein kinase kinase kinase kinase 4
-1.94	Hs.181107 annexin A13
-1.94	Hs.66392 intersectin 1 (SH3 domain protein)
-1.94	Hs.3781 similar to murine leucine-rich repeat protein
-1.90	Hs.1265 branched chain keto acid dehydrogenase E1, beta polypeptide (maple syrup urine disease)
-1.89	Hs.957 putative opioid receptor, neuromedin K (neurokinin B) receptor-like
-1.86	Hs.283330 hypothetical protein PRO1843
-1.82	Hs.249727 hypothetical protein FLJ11798
-1.81	Hs.82685 CD47 antigen (Rh-related antigen, integrin-associated signal transducer)
-1.79	Hs.184860 CGI-203 protein
-1.74	Hs.212587 Homo sapiens mRNA; cDNA DKFZp566M043 (from clone DKFZp566M043)

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

UP REGULATED IN FUGETAXIS COMPARED TO MEDIUM SDF-1 GRADIENTS

45.94	Hs.80358 SMC (mouse) homolog, Y chromosome
42.44	Hs.180911 ribosomal protein S4, Y-linked
28.32	Hs.99120 DEADH (Asp-Glu-Ala-AspHis) box polypeptide, Y chromosome
13.76	Hs.155397 Homo sapiens mRNA; cDNA DKFZp564K143 (from clone DKFZp564K143)
10.45	Hs.193145 ubiquitin specific protease 9, Y chromosome (Drosophila fat facets related)
10.07	Hs.155103 eukaryotic translation initiation factor 1A, Y chromosome
8.93	Hs.78913 chemokine (C-X3-C) receptor 1
8.52	Hs.2014 T cell receptor delta locus
7.9	Hs.100000 S100 calcium-binding protein A8 (calgranulin A)
7.3	Hs.99120 DEADH (Asp-Glu-Ala-AspHis) box polypeptide, Y chromosome
6.58	Hs.3195 small inducible cytokine subfamily C, member 1 (lymphotactin)
6.36	Hs.73931 major histocompatibility complex, class II, DQ beta 1
6.02	Hs.75184 chitinase 3-like 1 (cartilage glycoprotein-39)
5.57	Hs.76536 transducin (beta)-like 1
5.25	Hs.194366 transthyretin (prealbumin, amyloidosis type I)
5.1	Hs.19413 S100 calcium-binding protein A12 (calgranulin C)
5.07	Hs.251419 Homo sapiens DNA sequence from PAC 845O24 on chromosome 1p36.1-36.2. Contains a gene for a Heterogenous Nuclear Ribonucleoprotein HNRNP C1 LIKE protein and four genes similar to Melanoma Preferentially Expressed Antigen PRAME and KIAA0014. Conta
5.01	Hs.156110 immunoglobulin kappa constant
4.97	gb:AF262973.1 /DEF=Homo sapiens killer cell immunoglobulin-like receptor 3DL1 (KIR3DL1) mRNA, KIR3DL1*00701 allele, complete cds.
4.9	Hs.326737 Homo sapiens, clone MGC:4655, mRNA, complete cds
4.84	Hs.50929 hypothetical protein FLJ13842
4.72	Hs.57975 calsequestrin 2 (cardiac muscle)
4.54	Hs.7358 hypothetical protein FLJ13110
4.51	Hs.177605 killer cell lectin-like receptor subfamily C, member 2
4.44	Hs.79691 LIM domain protein
4.33	Hs.37142 ephrin-A5
4.31	Hs.198396 ATP-binding cassette, sub-family A (ABC1), member 4
4.29	Hs.179665 cyclin-dependent kinase inhibitor 1A (p21, Cip1)
4.15	Hs.8108 disabled (Drosophila) homolog 1
4.15	Hs.54481 low density lipoprotein receptor-related protein 8, apolipoprotein e receptor
4	Hs.77436 pleckstrin
4	Hs.44278 hypothetical protein FLJ12538 similar to ras-related protein RAB17
3.91	Hs.123030 Human kappa-immunoglobulin germline pseudogene (Chr22.4) variable region (subgroup V kappa II)
3.89	Hs.2730 heterogeneous nuclear ribonucleoprotein L
3.87	Hs.7936 BAI1-associated protein 2
3.85	Hs.112278 arrestin, beta 1
3.82	Hs.75573 centromere protein E (312kD)
3.82	gb:NM_000961.1 /DEF=Homo sapiens prostaglandin I2 (prostacyclin) synthase (PTGIS), mRNA.
3.82	Hs.79706 plectin 1, intermediate filament binding protein, 500kD
3.8	Hs.56336 protein kinase, Y-linked
3.79	Hs.306691 Homo sapiens cDNA: FLJ20915 fis, clone ADSE00692
3.76	Hs.182740 ribosomal protein S11
3.76	Hs.9873 likely homolog of rat kinase D-interacting substance of 220 kDa; KIAA1250 protein
3.69	Hs.199250 chloride channel 4
3.66	gb:NM_030615.1 /DEF=Homo sapiens kinesin-like 3 (KNSL3), transcript variant 1, mRNA.
3.66	Hs.10235 chromosome 5 open reading frame 4
3.62	Hs.313951 ESTs
3.6	Hs.294158 tryptase beta 2
3.6	Hs.307187 H.sapiens mRNA for soluble delta TCR
3.57	Hs.132560 hypothetical protein FLJ10312
3.56	Hs.272366 Homo sapiens partial IGVH3 gene for immunoglobulin heavy chain V region, case 2, cell E 172
3.55	Hs.8850 a disintegrin and metalloproteinase domain 12 (meltrin alpha)
3.55	Hs.21486 signal transducer and activator of transcription 1, 91kD
3.54	gb:AF263617.1 /DEF=Homo sapiens killer cell immunoglobulin-like receptor 3DL2 (KIR3DL2) mRNA, KIR3DL2*00901 allele, complete cds.

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

3.53	Hs.169910 KIAA0173 gene product
3.52	Hs.250502 carbonic anhydrase VIII
3.5	Hs.2352 adenylate cyclase 2 (brain)
3.5	gb:M32577.1 /DEF=Human MHC HLA-DQ beta mRNA, complete cds.
3.48	Hs.269926 Homo sapiens cDNA: FLJ21441 fis, clone COL04422
3.47	Hs.155103 eukaryotic translation initiation factor 1A, Y chromosome
3.45	Hs.171814 parathymosin
3.42	Hs.203846 TEA domain family member 3
3.42	Hs.2142 5-hydroxytryptamine (serotonin) receptor 3A
3.38	Hs.14642 chromosome 16 open reading frame 3
3.38	Hs.76722 CCAATenhancer binding protein (CEBP), delta
3.36	Hs.64311 a disintegrin and metalloproteinase domain 17 (tumor necrosis factor, alpha, converting enzyme)
3.35	Hs.177961 Human Chromosome 16 BAC clone CIT987SK-A-388D4
3.35	Hs.153985 solute carrier family 7 (cationic amino acid transporter, y+ system), member 2
3.35	Hs.137569 tumor protein 63 kDa with strong homology to p53
3.34	Hs.132942 GTPase regulator associated with the focal adhesion kinase pp125(FAK); KIAA0621 protein
3.32	Hs.278962 AIM-1 protein
3.31	Hs.104624 aquaporin 9
3.29	Hs.12079 calsyntenin-2
3.28	Hs.326198 transcription factor 4
3.24	Hs.127384 DKFZP564C196 protein
3.18	Hs.257174 hypothetical protein FLJ10601
3.17	granulysin
3.16	Hs.171596 EphA2
3.15	gb:NM_030773.1 /DEF=Homo sapiens beta tubulin 1, class VI (TUBB1), mRNA.
3.15	Hs.75137 KIAA0193 gene product
3.11	natriuretic peptide receptor A/guanylate cyclase A (atrionatriuretic peptide receptor A)
3.1	Hs.164960 BarH-like homeobox 1
3.09	Hs.181581 glutamate receptor, ionotropic, kainate 1
3.07	Hs.82112 interleukin 1 receptor, type I
3.05	Hs.287662 Homo sapiens cDNA: FLJ21424 fis, clone COL04157
3.03	Hs.130546 hypothetical protein FLJ20449
3.03	Hs.2014 T cell receptor delta locus
3.02	Hs.75617 collagen, type IV, alpha 2
3	Hs.58014 G protein-coupled receptor, family C, group 5, member C
2.99	Hs.118695 potassium voltage-gated channel, subfamily G, member 1
2.99	Hs.247741 protocadherin alpha 2
2.98	Hs.13040 G protein-coupled receptor 86
2.98	Hs.69319 CA11
2.98	Hs.146409 cell division cycle 42 (GTP-binding protein, 25kD)
2.97	Hs.79876 steroid sulfatase (microsomal), arylsulfatase C, isozyme S
2.96	Hs.325722 immunoglobulin kappa variable 3D-15
2.93	Hs.284277 Homo sapiens immunoglobulin mu chain antibody MO30 (IgM) mRNA, complete cds
2.87	gb:AF349720.1 /DEF=Homo sapiens magphinin beta (TRO) mRNA, complete cds.
2.82	Hs.79706 plectin 1, intermediate filament binding protein, 500kD
2.79	Hs.694 interleukin 3 (colony-stimulating factor, multiple)
2.79	Hs.131361 pyruvate dehydrogenase (lipoamide) alpha 2
2.74	Hs.265848 similar to rat myomegalin
2.72	Hs.274230 3-phosphoadenosine 5-phosphosulfate synthase 2
2.72	Hs.306643 Homo sapiens cDNA FLJ13302 fis, clone OVARC1001357
2.71	Hs.153837 myeloid cell nuclear differentiation antigen
2.71	Hs.621 lectin, galactoside-binding, soluble, 3 (galectin 3)
2.69	Hs.227751 lectin, galactoside-binding, soluble, 1 (galectin 1)
2.69	Hs.84152 cystathionine-beta-synthase
2.69	Hs.48778 niban protein
2.68	Hs.158315 interleukin 18 receptor accessory protein
2.67	Hs.8074 brain-specific angiogenesis inhibitor 3
2.66	Hs.1915 folate hydrolase (prostate-specific membrane antigen) 1

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

2.66	Hs.24322 ATPase, H+ transporting, lysosomal (vacuolar proton pump) 9kD
2.64	Hs.18387 transcription factor AP-2 alpha (activating enhancer-binding protein 2 alpha)
2.63	Hs.118786 metallothionein 2A
2.62	Hs.119571 collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)
2.59	Hs.10086 type I transmembrane protein Fn14
2.59	Hs.22599 atrophin-1 interacting protein 1; activin receptor interacting protein 1
2.59	Hs.8982 ESTs, Highly similar to KIAA1395 protein H.sapiens
2.54	Hs.235935 nephroblastoma overexpressed gene
2.53	Hs.44205 cortistatin
2.52	Hs.692 tumor-associated calcium signal transducer 1
2.52	Hs.31792 hypothetical protein FLJ11082
2.52	Hs.282693 ESTs
2.51	Hs.223014 antizyme inhibitor
2.5	Hs.96744 prostate androgen-regulated transcript 1
2.5	Hs.41696 keratin, hair, acidic,1
2.49	Hs.184915 zinc finger protein, Y-linked
2.48	Hs.156346 topoisomerase (DNA) II alpha (170kD)
2.48	Hs.123079 Glutamate transporter II variant BHBGT IIB {5 region} human, brain and spinal cord, mRNA Partial Mutant, 129 nt
2.48	Hs.74085 DNA segment on chromosome 12 (unique) 2489 expressed sequence
2.47	Hs.248189 keratin, hair, acidic, 6
2.46	Hs.76807 major histocompatibility complex, class II, DR alpha
2.46	Hs.157429 SRY (sex determining region Y)-box 3
2.46	Hs.274691 adenylate kinase 3
2.42	Hs.286079 spinocerebellar ataxia 8
2.38	Hs.103124 ATPase, Ca++ transporting, plasma membrane 3
2.38	Hs.90821 ryanodine receptor 2 (cardiac)
2.34	Hs.82101 pleckstrin homology-like domain, family A, member 1
2.3	Hs.88411 lymphocyte antigen 117
2.29	Hs.29287 retinoblastoma-binding protein 8
2.29	Hs.301839 intracellular antigen detected by monoclonal antibody Ki-1; intracellular hyaluronan-binding protein
2.28	Hs.294158 tryptase beta 2
2.28	Hs.308026 major histocompatibility complex, class II, DR beta 5
2.27	Hs.128749 alpha-methylacyl-CoA racemase
2.27	Hs.77202 protein kinase C, beta 1
2.26	Hs.54481 low density lipoprotein receptor-related protein 8, apolipoprotein e receptor
2.25	Hs.258580 purinergic receptor P2X, ligand-gated ion channel, 2
2.25	Hs.78944 regulator of G-protein signalling 2, 24kD
2.24	Hs.88411 lymphocyte antigen 117
2.24	Hs.166186 chordin
2.24	Hs.284244 fibroblast growth factor 2 (basic)
2.22	Hs.77886 lamin AC
2.22	Hs.110637 homeo box A10
2.22	Hs.76136 thioredoxin
2.21	Hs.89472 angiotensin receptor 1
2.21	Hs.7242 Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 35907
2.2	Hs.201737 hypothetical protein FLJ14050
2.2	Hs.24385 Human hbc647 mRNA sequence
2.2	Hs.154762 HIV-1 rev binding protein 2
2.19	Hs.159971 SWISNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1
2.19	Hs.62954 ferritin, heavy polypeptide 1
2.18	Hs.201776 zinc finger, imprinted 2
2.18	Hs.272376 olfactory receptor, family 1, subfamily A, member 1
2.18	Hs.280380 aminopeptidase
2.18	Hs.267819 protein phosphatase 1, regulatory (inhibitor) subunit 2
2.17	Hs.105115 absent in melanoma 2
2.16	Hs.121084 eppin-3
2.16	Hs.293205 ESTs, Weakly similar to BC39498 1 H.sapiens

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

2.15	Hs.97084 lymphocyte antigen 94 (mouse) homolog (activating NK-receptor ; NK-p46)
2.15	Hs.93728 pre-B-cell leukemia transcription factor 2
2.14	Hs.89394 POU domain, class 1, transcription factor 1 (Pit1, growth hormone factor 1)
2.14	Hs.246107 elongation of very long chain fatty acids (FEN1Elo2, SUR4Elo3, yeast)-like 2
2.14	Hs.226025 vacuolar protein sorting 45A (yeast homolog)
2.14	Hs.69547 myelin basic protein
2.14	Hs.311 phosphoribosyl pyrophosphate amidotransferase
2.13	Hs.88411 lymphocyte antigen 117
2.13	Hs.287431 hypothetical protein FLJ11598
2.13	Hs.278486 olfactory receptor, family 1, subfamily E, member 2
2.13	Hs.8349 Apobec-1 complementation factor; APOBEC-1 stimulating protein
2.13	Hs.77436 pleckstrin
2.12	Hs.306955 Homo sapiens rab3 interacting protein variant 6 mRNA, partial cds
2.12	Hs.821 biglycan
2.11	Hs.288771 DKFZP586A0522 protein
2.1	Hs.225641 hypothetical protein FLJ13171
2.1	Hs.75825 pleiomorphic adenoma gene-like 1
2.09	Hs.241570 tumor necrosis factor (TNF superfamily, member 2)
2.08	Hs.727 inhibin, beta A (activin A, activin AB alpha polypeptide)
2.08	Hs.164371 hypothetical protein FLJ12439
2.08	Hs.94210 eyes absent (Drosophila) homolog 1
2.08	Hs.306455 Homo sapiens mRNA; cDNA DKFZp434K1126 (from clone DKFZp434K1126)
2.07	Hs.69049 tocopherol (alpha) transfer protein (ataxia (Friedreich-like) with vitamin E deficiency)
2.07	Hs.181353 UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2
2.06	Hs.171811 adenylate kinase 2
2.05	Hs.84298 CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated)
2.04	gb:K03226.1 /DEF=Human preprourokinase mRNA, complete cds.
2.04	Hs.858 v-rel avian reticuloendotheliosis viral oncogene homolog B (nuclear factor of kappa light polypeptide gene enhancer in B-cells 3)
2.03	Hs.41707 heat shock 27kD protein 3
2.03	Hs.150443 KIAA0320 protein
2.03	Hs.64639 glioma pathogenesis-related protein
2.03	Hs.77910 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1 (soluble)
2.03	Hs.3844 LIM domain only 4
2.02	Hs.288869 nuclear receptor subfamily 2, group F, member 2
2.02	Hs.36766 HT017 protein
2.02	Hs.1076 small proline-rich protein 1B (cornifin)
2.02	Hs.306711 Homo sapiens cDNA: FLJ21215 fis, clone COL00526
2.02	Hs.479 RAB5C, member RAS oncogene family
2.01	Hs.78672 laminin, alpha 4
2.01	Hs.164568 fibroblast growth factor 7 (keratinocyte growth factor)
2.01	Hs.102471 KIAA0680 gene product
2	Hs.143212 cystatin F (leukocystatin)
2	Hs.29352 tumor necrosis factor, alpha-induced protein 6
2	Hs.153924 death-associated protein kinase 1
2	Hs.182575 solute carrier family 15 (H+peptide transporter), member 2
1.99	Hs.158330 neuropeptide Y receptor Y5
1.99	Hs.169246 melanoma antigen, family A, 12
1.99	Hs.6580 Homo sapiens cDNA: FLJ23227 fis, clone CAE00645, highly similar to AF052138 Homo sapiens clone 23718 mRNA sequence
1.98	Hs.35101 proline-rich Gla (G-carboxyglutamic acid) polypeptide 2
1.98	Hs.41270 procollagen-lysine, 2-oxoglutarate 5-dioxygenase (lysine hydroxylase) 2
1.97	Hs.13046 thioredoxin reductase 1
1.97	Hs.2667 metallothionein 1H
1.96	Hs.1481 histidine decarboxylase
1.96	Hs.100194 arachidonate 5-lipoxygenase-activating protein
1.95	Hs.41143 phosphoinositide-specific phospholipase C-beta 1
1.94	Hs.166072 annexin A2 pseudogene 2

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

1.94	Hs.295112 KIAA0618 gene product
1.94	— M24537B subtilis pheB, pheA genes corresponding to nucleotides 2017-3334 of M24537 (-5, -M, -3 represent transcript regions 5 prime, Middle, and 3 prime respectively)
1.94	Hs.48778 niban protein
1.93	Hs.29206 Homo sapiens clone 24659 mRNA sequence
1.93	gb:J04755.1 /DEF=Human ferritin H processed pseudogene, complete cds.
1.92	Hs.306508 Homo sapiens mRNA; cDNA DKFZp762O1415 (from clone DKFZp762O1415)
1.92	Hs.13223 Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 51358
1.92	Hs.21838 hypothetical protein FLJ11191
1.91	Hs.211585 6-phosphofructo-2-kinasefructose-2,6-biphosphatase 2
1.91	Hs.7358 hypothetical protein FLJ13110
1.91	Hs.195175 CASP8 and FADD-like apoptosis regulator
1.9	Hs.848 FK506-binding protein 4 (59kD)
1.9	Hs.2090 prostaglandin E receptor 2 (subtype EP2), 53kD
1.89	Hs.288983 hypothetical protein FLJ21477
1.89	Hs.50947 T-box 5
1.88	Hs.217493 annexin A2
1.88	Hs.306322 Homo sapiens mRNA; cDNA DKFZp566D153 (from clone DKFZp566D153)
1.88	Hs.158688 KIAA0741 gene product
1.87	Hs.282847 pregnancy specific beta-1-glycoprotein 3
1.87	Hs.239764 /len=924
1.87	Hs.217493 annexin A2
1.87	Hs.217493 annexin A2
1.86	Hs.1521 immunoglobulin mu binding protein 2
1.86	Hs.18878 hypothetical protein FLJ21620
1.85	Hs.302022 PR domain containing 16
1.85	erythropoietin receptor
1.85	Hs.173451 metallothionein 1G
1.85	Hs.293266 sperm protein associated with the nucleus, X chromosome, family member A1
1.84	Hs.180919 inhibitor of DNA binding 2, dominant negative helix-loop-helix protein
1.83	Hs.98303 caveolin 3
1.83	Hs.283725 hypothetical protein FLJ12627
1.83	Hs.274509 T cell receptor gamma constant 2
1.83	Hs.306305 Homo sapiens mRNA; cDNA DKFZp564L102 (from clone DKFZp564L102)
1.83	Hs.119285 /len=716
1.83	Hs.107526 UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 5
1.82	Hs.112259 T cell receptor gamma locus
1.82	Hs.195175 CASP8 and FADD-like apoptosis regulator
1.82	Hs.132781 class I cytokine receptor
1.82	Hs.326392 son of sevenless (Drosophila) homolog 1
1.81	Hs.77886 lamin AC
1.8	Hs.287445 hypothetical protein FLJ11726
1.8	Homo sapiens mRNA; cDNA DKFZp586D0918 (from clone DKFZp586D0918)
1.79	intersectin 1 (SH3 domain protein)
1.79	Hs.272564 muscle disease-related protein
1.79	Hs.88474 prostaglandin-endoperoxide synthase 1 (prostaglandin GH synthase and cyclooxygenase)
1.78	Hs.112259 T cell receptor gamma locus
1.78	gb:NM_031286.1 /DEF=Homo sapiens SH3BGRL3-like protein (SH3BGRL3), mRNA.
1.77	Hs.287388 histamine H4 receptor
1.77	Hs.211556 hypothetical protein MGC5487
1.77	Hs.195175 CASP8 and FADD-like apoptosis regulator
1.77	Hs.248183 olfactory receptor, family 1, subfamily G, member 1
1.77	Hs.273294 hypothetical protein FLJ20069
1.77	KIAA0674 protein
1.76	growth arrest and DNA-damage-inducible 34
1.76	Hs.110915 interleukin 22 receptor
1.76	Hs.102471 KIAA0680 gene product
1.75	Hs.75825 pleiomorphic adenoma gene-like 1

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

1.75	Hs.61152 exostoses (multiple)-like 2
1.75	Hs.195175 CASP8 and FADD-like apoptosis regulator
1.75	Hs.194019 attractin
1.74	Hs.2200 perforin 1 (pore forming protein)
1.74	Hs.1334 v-myb avian myeloblastosis viral oncogene homolog
1.74	Hs.217493 annexin A2
1.74	Hs.293934 major histocompatibility complex, class II, DR beta 4
1.74	Hs.142023 T cell activation, increased late expression
1.73	gb:NM_031283.1 /DEF=Homo sapiens HMG-box transcription factor TCF-3 (TCF-3), mRNA.
1.73	Hs.122939 /len=646
1.73	Hs.80758 aspartyl-tRNA synthetase
1.73	Hs.270010 KIAA0508 protein
1.72	Hs.169222 acrosomal vesicle protein 1
1.72	Hs.6654 KIAA0657 protein
1.72	Hs.73291 hypothetical protein FLJ10881
1.71	Hs.50964 carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)
1.71	Hs.250615 cytochrome P450, subfamily IIA (phenobarbital-inducible), polypeptide 7
1.71	Hs.153445 Human mRNA for unknown product, partial cds
1.71	Hs.112259 T cell receptor gamma locus
1.71	Hs.272327 Homo sapiens mRNA; cDNA DKFZp434K0423 (from clone DKFZp434K0423); partial cds
1.71	Hs.76536 transducin (beta)-like 1
1.71	3-phosphoinositide dependent protein kinase-1
1.71	Hs.198281 pyruvate kinase, muscle
1.71	Hs.177543 antigen identified by monoclonal antibodies 12E7, F21 and O13
1.7	Hs.195175 CASP8 and FADD-like apoptosis regulator
1.7	Hs.154868 carbamoyl-phosphate synthetase 2, aspartate transcarbamylase, and dihydroorotase
1.7	Hs.289053 hypothetical protein FLJ12474

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

DOWN REGULATED IN FUGETAXIS COMPARED TO MEDIUM SDF-1 GRADIENTS

-21.97	Hs.323342 actin related protein 23 complex, subunit 4 (20 kD)
-13.79	Hs.78409 collagen, type XVIII, alpha 1
-11.21	Hs.46907 HEMK homolog 7kb
-9.32	Hs.15075 hypothetical protein DKFZp434E2216
-8.93	Hs.93597 cyclin-dependent kinase 5, regulatory subunit 1 (p35)
-8.88	Hs.85752 uncharacterized hematopoietic stemprogenitor cells protein MDS026
-8.84	Hs.29222 zinc finger protein 76 (expressed in testis)
-8.32	Hs.53155 properdin P factor, complement
-7.73	Hs.289031 hypothetical protein FLJ11848
-7.72	Hs.76845 phosphoserine phosphatase-like
-7.62	Hs.279881 alpha 1,2-mannosidase
-7.44	DOM-3 (C. elegans) homolog Z
-7.43	Hs.74047 electron-transfer-flavoprotein, beta polypeptide
-7.38	Hs.154797 KIAA0090 protein
-7.32	Hs.305960 hemoglobin, gamma A
-7.3	Hs.6051 KIAA0616 protein
-7.18	Hs.25477 hypothetical protein FLJ21044 similar to Rbig1
-7.05	Hs.306434 Homo sapiens mRNA for LST-1N protein
-7.03	Hs.76289 biliverdin reductase B (flavin reductase (NADPH))
-7.01	Hs.109441 hypothetical protein FLJ20707
-6.51	Hs.238679 Rag D protein
-6.47	Hs.38628 hypothetical protein
-6.41	Hs.3743 matrix metalloproteinase 24 (membrane-inserted)
-6.33	Hs.198161 phospholipase A2, group IVB (cytosolic)
-6.3	Hs.306781 Homo sapiens cDNA: FLJ21535 fis, clone COL06131
-6.15	Hs.205450 hypothetical protein FLJ22570
-6.12	Hs.155979 KIAA0295 protein
-6.06	Hs.12142 WD repeat domain 13
-6.04	Hs.99603 hypothetical protein FLJ13134
-5.79	Hs.226396 hypothetical protein FLJ11126
-5.53	Hs.23796 odz (odd Ozten-m, Drosophila) homolog 1
-5.51	Hs.306913 Homo sapiens cDNA: FLJ23564 fis, clone LNG10773
-5.37	Hs.279862 cdk inhibitor p21 binding protein
-5.33	Hs.8128 phosphatidylserine decarboxylase
-5.32	Hs.26045 protein tyrosine phosphatase, receptor type, A
-5.13	Hs.202955 hypothetical protein FLJ20507
-5.01	Hs.14142 nudix (nucleoside diphosphate linked moiety X)-type motif 2
-4.97	Hs.79340 PTH-responsive osteosarcoma B1 protein
-4.96	Hs.36977 hemoglobin, delta
-4.92	Hs.278483 H4 histone family, member E
-4.9	Hs.97176 hypothetical protein FLJ13906 similar to RING finger protein
-4.9	Hs.2399 matrix metalloproteinase 14 (membrane-inserted)
-4.85	Hs.78146 plateletendothelial cell adhesion molecule (CD31 antigen)
-4.8	Hs.12820 SnRNP assembly defective 1 homolog
-4.8	Hs.129903 polymerase (DNA-directed), lambda
-4.8	Hs.7943 RPB5-mediating protein
-4.78	Hs.326457 ESTs
-4.75	Hs.325530 KIAA1067 protein
-4.64	Hs.197335 plasma glutamate carboxypeptidase
-4.56	Hs.6092 f-box and leucine-rich repeat protein 2
-4.55	Hs.159241 polycystic kidney disease 2-like 1
-4.47	Hs.99987 excision repair cross-complementing rodent repair deficiency, complementation group 2 (xeroderma pigmentosum D)
-4.45	Hs.155204 zinc finger protein 174
-4.42	Hs.11135 major histocompatibility complex, class II, DN alpha
-4.39	Hs.20017 chromosome 22 open reading frame 4

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

-4.39	gb:M24668.1 /DEF=Human Ig rearranged H-chain V-region mRNA (C-D-JH4), complete cds.
-4.31	Hs.156115 potassium voltage-gated channel, KQT-like subfamily, member 1
-4.28	Hs.97574 exosome component Rrp41
-4.28	Hs.168737 ESTs, Highly similar to 2AAB_HUMAN SERINETHREONINE PROTEIN PHOSPHATASE 2A, 65 KDA REGULATORY SUBUNIT A, BETA ISOFORM H.sapiens
-4.22	Hs.300772 tropomyosin 2 (beta)
-4.2	Hs.283404 organic cation transporter
-4.19	Hs.103839 erythrocyte membrane protein band 4.1-like 3
-4.18	Hs.101874 mouse double minute 4, human homolog of; p53-binding protein
-4.13	Hs.33818 RecQ protein-like 5
-4.1	Hs.121102 vanin 2
-4.09	Hs.22370 Homo sapiens mRNA; cDNA DKFZp564O0122 (from clone DKFZp564O0122)
-4.06	Hs.36 lymphotoxin alpha (TNF superfamily, member 1)
-4.06	M10098 Human 18S rRNA sequence, length 1969 bases, middle target bases 647-1292
-4.05	Hs.79386 leiomodin 1 (smooth muscle)
-4.02	Hs.110796 SAR1 protein
-4.01	Hs.14286 flavin containing monooxygenase 5
-3.99	Hs.272108 ESTs
-3.98	Hs.112751 KIAA0892 protein
-3.98	Hs.47822 Rho guanine exchange factor (GEF) 11
-3.96	Hs.90443 NADH dehydrogenase (ubiquinone) Fe-S protein 8 (23kD) (NADH-coenzyme Q reductase)
-3.94	Hs.7426 KIAA0841 protein
-3.9	Hs.154085 leucine zipper protein 1
-3.89	gb:NM_030925.1 /DEF=Homo sapiens hypothetical protein FLJ12577 (FLJ12577), mRNA.
-3.86	Hs.102867 sodium-dependent high-affinity dicarboxylate transporter 3
-3.81	gb:BC006441.1 /DEF=Homo sapiens, Similar to RNA polymerase I transcription factor RRN3, clone MGC:13169, mRNA, complete cds.
-3.81	Hs.9857 carbonyl reductase
-3.79	Hs.119498 thyroid hormone receptor interactor 6
-3.77	Hs.194148 v-yes-1 Yamaguchi sarcoma viral oncogene homolog 1
-3.76	Hs.277401 bromodomain adjacent to zinc finger domain, 2A
-3.75	Hs.78921 A kinase (PRKA) anchor protein 1
-3.74	Hs.278064 Homo sapiens cDNA: FLJ23327 fis, clone HEP12630, highly similar to HSZNF37 Homo sapiens ZNF37A mRNA for zinc finger protein
-3.73	gb:NM_030930.1 /DEF=Homo sapiens unc93 (C.elegans) homolog B (UNC93B), mRNA.
-3.7	Hs.1265 branched chain keto acid dehydrogenase E1, beta polypeptide (maple syrup urine disease)
-3.69	Hs.48269 vaccinia related kinase 1
-3.66	Hs.168670 peroxisomal farnesylated protein
-3.66	Hs.155597 D component of complement (adipsin)
-3.66	Hs.291972 ESTs, Moderately similar to SC14_HUMAN SEC14-LIKE PROTEIN H.sapiens
-3.64	Hs.13405 gephyrin
-3.64	Hs.7019 signal-induced proliferation-associated gene 1
-3.61	Hs.285005 mitochondrial import receptor Tom22
-3.61	Hs.210546 interleukin 21 receptor
-3.58	KIAA1117 protein
-3.57	Hs.44865 lymphoid enhancer binding factor-1
-3.57	Hs.23585 KIAA1078 protein
-3.56	Hs.14846 Homo sapiens mRNA; cDNA DKFZp564D016 (from clone DKFZp564D016)
-3.56	Hs.47344 advillin
-3.55	Hs.296821 Human facioscapulohumeral muscular dystrophy (FSHD) gene region, D4Z4 tandem repeat unit
-3.53	Hs.2558 bone gamma-carboxyglutamate (gla) protein (osteocalcin)
-3.52	Hs.80741 propionyl Coenzyme A carboxylase, alpha polypeptide
-3.47	Hs.59544 excision repair cross-complementing rodent repair deficiency, complementation group 1 (includes overlapping antisense sequence)
-3.47	Hs.248007 Human beta-cytoplasmic actin (ACTBP9) pseudogene
-3.47	Hs.300496 mitochondrial solute carrier
-3.45	Hs.111244 hypothetical protein
-3.44	Hs.193716 complement component (3b4b) receptor 1, including Knops blood group system
-3.37	Hs.79064 deoxyhypusine synthase

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

-3.36	Hs.5378 spondin 1, (f-spondin) extracellular matrix protein
-3.35	Hs.94229 hypothetical protein FLJ11939
-3.33	gb:M24669.1 /DEF=Human Ig rearranged H-chain V-region mRNA (C-D-JH6), complete cds.
-3.33	Hs.16193 Homo sapiens mRNA; cDNA DKFZp586B211 (from clone DKFZp586B211)
-3.32	Hs.5353 caspase 10, apoptosis-related cysteine protease
-3.32	Hs.117242 meningioma expressed antigen 6 (coiled-coil proline-rich)
-3.3	Hs.5378 spondin 1, (f-spondin) extracellular matrix protein
-3.29	Hs.203269 ESTs, Moderately similar to ALU8_HUMAN ALU SUBFAMILY SX SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens
-3.27	Hs.184523 KIAA0965 protein
-3.27	Homo sapiens chromosome 19, cosmid R28784, complete sequence.
-3.26	Hs.21542 KIAA1035 protein
-3.26	Hs.83765 dihydrofolate reductase
-3.25	Hs.283860 Homo sapiens partial mRNA for MOZCBP chimeric transcript type II
-3.24	Hs.168625 androgen-induced prostate proliferative shutoff associated protein
-3.24	Hs.9846 KIAA1040 protein
-3.23	Hs.104916 hypothetical protein FLJ21940
-3.22	gb:BC006222.1 /DEF=Homo sapiens, clone MGC:10279, mRNA, complete cds.
-3.21	Hs.73980 troponin T1, skeletal, slow
-3.2	Hs.85195 myeloid leukemia factor 1
-3.19	Hs.288697 hypothetical protein MGC11349
-3.17	Hs.26899 KIAA0285 gene product
-3.17	Hs.262869 plasminogen-like
-3.16	Hs.226581 COX15 (yeast) homolog, cytochrome c oxidase assembly protein
-3.16	Hs.4854 cyclin-dependent kinase inhibitor 2C (p18, inhibits CDK4)
-3.15	Hs.184938 Novel human gene mapping to chomosome 13
-3.15	Hs.44697 ATPase, Class V, type 10C
-3.14	Hs.25155 neuroepithelial cell transforming gene 1
-3.13	Hs.267263 hypothetical protein
-3.13	Hs.21361 KIAA1023 protein
-3.11	Hs.180686 ubiquitin protein ligase E3A (human papilloma virus E6-associated protein, Angelman syndrome)
-3.11	Hs.86178 M-phase phosphoprotein 9
-3.1	
-3.08	Hs.31324 zinc finger protein 155 (pHZ-96)
-3.06	Hs.61712 pyruvate dehydrogenase kinase, isoenzyme 1
-3.06	Hs.103839 erythrocyte membrane protein band 4.1-like 3
-3.06	Hs.292998 ESTs
-3.05	Hs.31476 Homo sapiens cDNA FLJ13872 fis, clone THYRO1001322
-3.04	Hs.26471 Homo sapiens clone HQ0692
-3.04	Hs.100602 MAD (mothers against decapentaplegic, Drosophila) homolog 7
-3.03	Hs.79993 peroxisomal biogenesis factor 7
-3.03	Hs.82919 cullin 2
-3.02	Hs.1975 hypothetical protein FLJ21007
-3.01	Hs.118738 KIAA0800 gene product
-3	Hs.222306 hypothetical protein MGC3329
-2.99	Hs.100090 tetraspan 3
-2.98	Hs.18889 DKFZP434M183 protein
-2.98	Hs.20019 hemochromatosis
-2.96	Hs.21811 hypothetical protein FLJ10374
-2.92	Hs.308332 ESTs, Highly similar to A42735 ribosomal protein L10, cytosolic H.sapiens
-2.9	Hs.9003 hypothetical protein FLJ13868
-2.89	Hs.234265 DKFZP586G011 protein
-2.88	Hs.26468 amyloid beta (A4) precursor protein-binding, family A, member 2 (X11-like)
-2.85	Hs.68398 period (Drosophila) homolog 1
-2.84	Hs.153639 hypothetical SBBI03 protein
-2.84	Hs.184019 Homo sapiens clone 23551 mRNA sequence
-2.82	Hs.5378 spondin 1, (f-spondin) extracellular matrix protein
-2.8	Hs.159900 G protein-coupled receptor 15

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

-2.8	Hs.6179 DEADH (Asp-Glu-Ala-AspHis) box polypeptide 17 (72kD)
-2.8	Hs.323664 nudix (nucleoside diphosphate linked moiety X)-type motif 6
-2.79	Hs.64096 KIAA0427 gene product
-2.78	Hs.94037 hypothetical protein FLJ23053
-2.75	Hs.74861 activated RNA polymerase II transcription cofactor 4
-2.74	Hs.78946 cullin 3
-2.74	Hs.292853 ESTs
-2.73	Hs.300772 tropomyosin 2 (beta)
-2.73	Hs.69745 ferredoxin reductase
-2.73	Hs.75694 mannose phosphate isomerase
-2.71	Hs.113 epoxide hydrolase 2, cytoplasmic
-2.71	Hs.112434 Novel human gene mapping to chomosome 13
-2.71	Hs.27371 Homo sapiens mRNA; cDNA DKFZp566J123 (from clone DKFZp566J123)
-2.7	Hs.287437 Homo sapiens cDNA FLJ11662 fis, clone HEMBA1004629
-2.69	gb:BC006241.1 /DEF=Homo sapiens, hypothetical protein FLJ10647, clone MGC:11318, mRNA, complete cds.
-2.67	Hs.301011 KIAA0876 protein
-2.66	Hs.142245 HERV-H LTR-associating 3
-2.65	Hs.283032 hypothetical protein PRO2015
-2.63	Hs.182595 dynein, axonemal, light polypeptide 4
-2.63	Hs.9071 progesterone membrane binding protein
-2.62	gb:U31110.1 /DEF=Human alternatively spliced trp-1 protein and unspliced trp-1 protein (trp-1) mRNA, complete cds.
-2.62	Hs.168670 peroxisomal farnesylated protein
-2.6	Hs.66191 Homo sapiens clone 24675 mRNA sequence
-2.6	Hs.9196 hypothetical protein
-2.58	Hs.184376 synaptosomal-associated protein, 23kD
-2.58	Hs.27610 retinoic acid- and interferon-inducible protein (58kD)
-2.57	Hs.77868 ORF
-2.57	Hs.77152 minichromosome maintenance deficient (S. cerevisiae) 7
-2.56	Hs.115537 putative dipeptidase
-2.54	Hs.2006 glutathione S-transferase M3 (brain)
-2.54	Hs.7854 zinciron regulated transporter-like
-2.53	Hs.19561 NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 7 (14.5kD, B14.5a)
-2.53	Hs.72980 Protein P3
-2.53	Hs.262023 Homo sapiens mRNA; cDNA DKFZp564N1623 (from clone DKFZp564N1623); complete cds
-2.53	Hs.79368 epithelial membrane protein 1
-2.52	Hs.23964 sin3-associated polypeptide, 18kD
-2.51	Hs.966 coilin
-2.5	Hs.15898 2,4-dienoyl CoA reductase 2, peroxisomal
-2.49	Hs.118722 fucosyltransferase 8 (alpha (1,6) fucosyltransferase)
-2.49	Hs.278503 regulated in glioma
-2.48	Hs.180338 tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein)
-2.48	Hs.46465 T-cell, immune regulator 1
-2.48	Hs.100915 peroxisomal biogenesis factor 16
-2.48	Hs.119274 RAS p21 protein activator (GTPase activating protein) 3 (Ins(1,3,4,5)P4-binding protein)
-2.46	Hs.50748 chromosome 21 open reading frame 18
-2.46	Hs.25155 neuroepithelial cell transforming gene 1
-2.46	Hs.108779 DKFZP586E1519 protein
-2.46	Hs.82527 sialyltransferase 8 (alpha-N-acetylneuraminate: alpha-2,8-sialytransferase, GD3 synthase) A
-2.46	Hs.99491 RAS guanyl releasing protein 2 (calcium and DAG-regulated)
-2.44	Hs.143131 glycoprotein A33 (transmembrane)
-2.42	gb:BC006332.1 /DEF=Homo sapiens, clathrin, light polypeptide (Lcb), clone MGC:12930, mRNA, complete cds.
-2.4	Hs.7594 solute carrier family 2 (facilitated glucose transporter), member 3
-2.4	Hs.15984 pp21 homolog
-2.39	Hs.78056 cathepsin L
-2.39	Hs.152981 CDP-diacylglycerol synthase (phosphatidate cytidylyltransferase) 1
-2.39	Hs.271699 polymerase (DNA directed) iota

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

-2.38	Hs.101299 cullin 5
-2.38	Hs.49994 Homo sapiens, clone MGC:10871, mRNA, complete cds
-2.35	Hs.211522 /len=545
-2.35	Hs.76297 G protein-coupled receptor kinase 6
-2.35	Hs.65648 RNA binding motif protein 8A
-2.34	Hs.109655 sex comb on midleg (Drosophila)-like 1
-2.33	Hs.6793 platelet-activating factor acetylhydrolase, isoform Ib, gamma subunit (29kD)
-2.32	Hs.29417 HCF-binding transcription factor Zhangfei
-2.31	gb:NM_031206.1 /DEF=Homo sapiens hypothetical protein FLJ12525 (FLJ12525), mRNA.
-2.31	Hs.29725 hypothetical protein FLJ13197
-2.31	Hs.278973 angiopoietin-3
-2.31	Hs.236642 3-hydroxyisobutyryl-Coenzyme A hydrolase
-2.31	Hs.111323 Protein inhibitor of activated STAT X
-2.3	Hs.15106 chromosome 14 open reading frame 1
-2.3	Hs.5022 imprinted in Prader-Willi syndrome
-2.29	Hs.13980 ubiquitously transcribed tetratricopeptide repeat gene, X chromosome
-2.28	Hs.306533 Untitled
-2.28	Hs.285737 Homo sapiens cDNA: FLJ20895 fis, clone ADKA03483
-2.27	Hs.183291 zinc finger protein 268
-2.27	Hs.82919 cullin 2
-2.26	Hs.5881 ELL gene (11-19 lysine-rich leukemia gene)
-2.26	Hs.294014 ESTs
-2.25	Hs.62187 phosphatidylinositol glycan, class K
-2.24	Hs.1117 tripeptidyl peptidase II
-2.22	Hs.153299 DOM-3 (C. elegans) homolog Z
-2.22	Hs.250619 phorbolin-like protein MDS019
-2.22	Hs.301114 zinc finger protein 79 (pT7)
-2.22	Hs.300741 sorcin
-2.21	Hs.295923 seven in absentia (Drosophila) homolog 1
-2.21	Hs.17775 p75NTR-associated cell death executor; ovarian granulosa cell protein (13kD)
-2.2	Hs.174185 ectonucleotide pyrophosphatasephosphodiesterase 2 (autotaxin)
-2.19	Hs.2864 early endosome antigen 1, 162kD
-2.19	Hs.321567 complexin 2
-2.19	Hs.31432 cardiac ankyrin repeat protein
-2.18	Hs.77508 glutamate dehydrogenase 1
-2.18	Hs.293495 ESTs, Weakly similar to ALU1_HUMAN ALU SUBFAMILY J SEQUENCE CONTAMINATION WARNING ENTRY H.sapiens
-2.17	Hs.48924 KIAA0512 gene product; ALEX2
-2.17	Hs.16079 hypothetical protein FLJ10233
-2.16	Hs.81424 ubiquitin-like 1 (sentrin)
-2.16	Hs.324730 glutathione S-transferase M1
-2.15	gb:AF019888.1 /DEF=Homo sapiens Arp23 complex 20 kDa subunit (ARC20) mRNA, complete cds.
-2.15	Hs.82143 E74-like factor 2 (ets domain transcription factor)
-2.13	Hs.76297 G protein-coupled receptor kinase 6
-2.13	Hs.241053 ESTs
-2.13	Hs.207805 Homo sapiens mRNA; cDNA DKFZp564I066 (from clone DKFZp564I066)
-2.13	Hs.193163 bridging integrator 1
-2.12	Hs.323820 Homo sapiens GL013 mRNA, complete cds
-2.12	Hs.194637 BANP homolog, SMAR1 homolog
-2.12	Hs.6657 /len=657
-2.12	Hs.920 modulator recognition factor I
-2.11	Hs.5997 hypothetical protein FLJ13078
-2.11	Hs.147916 DEADH (Asp-Glu-Ala-AspHis) box polypeptide 3
-2.11	Hs.237146 hypothetical protein FLJ12752
-2.11	Hs.7236 CGI-25 protein
-2.1	Hs.3530 TLS-associated serine-arginine protein 2
-2.1	Hs.221040 HBS1 (S. cerevisiae)-like
-2.1	Hs.322645 Homo sapiens mRNA; cDNA DKFZp586J101 (from clone DKFZp586J101)

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

-2.09	Hs.57553 tousled-like kinase 2
-2.08	Hs.71746 hypothetical protein FLJ11583
-2.08	Hs.234898 /len=382
-2.07	gb:AF356353.1 /DEF=Homo sapiens spindlin-like protein 2 (SPIN2) mRNA, complete cds.
-2.06	Hs.23240 Homo sapiens cDNA FLJ13496 fis, clone PLACE1004471, weakly similar to ZINC FINGER PROTEIN 83
-2.06	Hs.282344 Homo sapiens cDNA FLJ13387 fis, clone PLACE1001136
-2.06	Hs.283709 lipopolysaccharide specific response-7 protein
-2.05	Hs.110796 SAR1 protein
-2.05	Hs.108947 KIAA0050 gene product
-2.04	Hs.271954 pan-hematopoietic expression
-2.04	Hs.279819 APR-1 protein
-2.03	Hs.279932 CGI-105 protein
-2.02	Hs.178011 hypothetical protein FLJ20257
-2.01	Hs.13225 UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 4
-2.01	Hs.180338 tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein)
-2.01	Hs.16193 Homo sapiens mRNA; cDNA DKFZp586B211 (from clone DKFZp586B211)
-2	Hs.7158 DKFZP566H073 protein
-2	Hs.5002 copper chaperone for superoxide dismutase
-2	Hs.279777 hypothetical protein
-1.99	Hs.264330 N-acylsphingosine amidohydrolase (acid ceramidase)-like
-1.97	Hs.9456 SWISNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5
-1.97	Hs.302114 Human DNA sequence from clone RP5-843L14 on chromosome 20. Contains ESTs, STSs and GSSs. Contains a novel gene and the 5 part of a gene for a novel protein similar to X-linked ribosomal protein 4 (RPS4X)
-1.97	Hs.102 aminomethyltransferase (glycine cleavage system protein T)
-1.97	Hs.75790 phosphatidylinositol glycan, class C
-1.96	Hs.180338 tumor necrosis factor receptor superfamily, member 12 (translocating chain-association membrane protein)
-1.95	Hs.81687 non-metastatic cells 3, protein expressed in
-1.93	Hs.31659 thyroid hormone receptor-associated protein, 95-kD subunit
-1.92	Hs.99847 peroxisome biogenesis factor 1
-1.92	Hs.46736 hypothetical protein FLJ23476
-1.92	Hs.77252 fragile histidine triad gene
-1.91	Hs.153022 TATA box binding protein (TBP)-associated factor, RNA polymerase I, C, 110kD
-1.91	Hs.66180 nucleosome assembly protein 1-like 2
-1.91	Hs.8198 zinc finger protein 204
-1.9	electron-transferring-flavoprotein dehydrogenase
-1.9	Hs.29288 hypothetical protein FLJ21865
-1.9	Hs.244 amino-terminal enhancer of split
-1.89	Hs.279902 cofactor required for Sp1 transcriptional activation, subunit 9 (33kD)
-1.89	Hs.119699 hypothetical protein FLJ12969
-1.89	Hs.156667 KIAA1536 protein
-1.88	Hs.48433 endocrine regulator
-1.88	Hs.8124 PH domain containing protein in retina 1
-1.87	Hs.293219 ESTs
-1.86	Hs.110298 hypothetical protein FLJ13322
-1.86	Human clone 23719 mRNA sequence
-1.86	Hs.152151 plakophilin 4
-1.86	Hs.24284 ADP-ribosyltransferase (NAD+; poly (ADP-ribose) polymerase)-like 2
-1.86	Hs.9884 spindle pole body protein
-1.85	Hs.122607 B-cell CLL/lymphoma 9
-1.85	Hs.7194 CGI-74 protein
-1.84	Hs.322478 KIAA0117 protein
-1.84	Hs.12835 A kinase (PRKA) anchor protein 7
-1.83	Hs.43803 leukocyte-associated Ig-like receptor 2
-1.83	Hs.66708 vesicle-associated membrane protein 3 (cellubrevin)
-1.82	Hs.249495 heterogeneous nuclear ribonucleoprotein A1

FIGURE 8

Table 6
Differential Gene Expression in Medium vs Fugetaxis SDF-1 Gradients

-1.82	Hs.266933 hect domain and RLD 2
-1.81	Hs.119000 actinin, alpha 1
-1.81	Hs.177486 amyloid beta (A4) precursor protein (protease nexin-II, Alzheimer disease)
-1.8	Hs.300684 calcitonin gene-related peptide-receptor component protein
-1.8	Hs.18490 hypothetical protein FLJ20452
-1.8	Hs.279785 putative secreted protein
-1.8	Hs.17409 cysteine-rich protein 1 (intestinal)
-1.79	Hs.301201 Homo sapiens cDNA FLJ14152 fis, clone MAMMA1003089
-1.79	Hs.16803 LUC7 (S. cerevisiae)-like
-1.79	Hs.265561 CD2-associated protein
-1.79	Hs.30696 transcription factor-like 5 (basic helix-loop-helix)
-1.79	Hs.46907 /len=607
-1.78	Hs.240112 KIAA0276 protein
-1.78	Hs.41072 serine (or cysteine) proteinase inhibitor, clade B (ovalbumin), member 6
-1.77	Hs.330056 hypothetical protein FLJ22795
-1.77	Hs.5353 caspase 10, apoptosis-related cysteine protease
-1.77	Hs.75061 macrophage myristoylated alanine-rich C kinase substrate
-1.77	gb:NM_031214.1 /DEF=Homo sapiens hypothetical protein (AF311304), mRNA.
-1.76	Hs.285848 KIAA1454 protein
-1.76	Hs.75692 asparagine synthetase
-1.75	Hs.36972 CD7 antigen (p41)
-1.75	Hs.83958 transducin-like enhancer of split 4, homolog of Drosophila E(sp1)
-1.75	Hs.64310 interleukin 11 receptor, alpha
-1.74	Hs.198726 vasoactive intestinal peptide receptor 1
-1.74	Hs.194329 hypothetical protein FLJ21174
-1.74	Hs.102456 survival of motor neuron protein interacting protein 1
-1.74	Hs.26471 Homo sapiens clone HQ0692
-1.74	Homo sapiens Chromosome 16 BAC clone CIT987SK-A-67A1, complete sequence.
-1.74	Hs.158195 heat shock transcription factor 2
-1.74	Hs.306173 phosphatidylinositol glycan, class C, pseudogene 1
-1.73	Hs.9452 KIAA0770 protein
-1.73	Hs.31834 Homo sapiens clone 25129 mRNA sequence
-1.73	Hs.77602 damage-specific DNA binding protein 2 (48kD)
-1.73	Hs.20952 Homo sapiens clone 24411 mRNA sequence
-1.73	Hs.9880 peptidyl prolyl isomerase H (cyclophilin H)
-1.72	Hs.236642 3-hydroxyisobutyryl-Coenzyme A hydrolase
-1.72	Hs.78409 collagen, type XVIII, alpha 1
-1.72	Hs.4764 KIAA0763 gene product
-1.72	Hs.1602 dihydropyrimidine dehydrogenase
-1.72	Hs.404 myeloidlymphoid or mixed-lineage leukemia (trithorax (Drosophila) homolog); translocated to, 3
-1.71	Hs.301667 Homo sapiens mRNA; cDNA DKFZp566I043 (from clone DKFZp566I043)
-1.71	Hs.180895 putative brain nuclearly-targeted protein
-1.71	Hs.128646 hypothetical protein FLJ20639
-1.71	Hs.184736 hypothetical protein FLJ10097
-1.71	Hs.9222 estrogen receptor binding site associated, antigen, 9
-1.7	Hs.30783 hypothetical protein FLJ20850
-1.7	Hs.110477 dolichyl-phosphate mannosyltransferase polypeptide 3

FIGURE 9

Table 7
Chemotaxis versus Fugetaxis: Downstream transcriptional changes

Actin/Cytoskeletal

Increased in Chemotaxis		Increased in Fugetaxis	
2.97	Spectrin beta, non-erythrocytic 1	3.05	Microtubule-associated protein, RPEB3
2.62	Myosin, light polypeptide 5, regulatory	2.81	Plectin 1, intermediate filament binding protein
2.52	Keratin 1	2.46	Microtubule-associated protein 1A like protein (MILP)
1.98	Plakophilin 4	2.20	Ankyrin 1, erythrocytic
1.81	Capping protein (actin filament), muscle	2.08	Capping protein (actin filament), gelsolin-like

ECM/Adhesion

Increased in Chemotaxis		Increased in Fugetaxis	
14.00	Collagen, type XVIII, alpha 1	11.00	Chitinase 3-like 1 (cartilage glycoprotein-39)
4.73	Spondin 1 (f-spondin)	3.71	Epithelial V-like antigen 1
3.47	CD31 adhesion molecule	2.99	Vascular endothelial growth factor (VEGF)
3.33	Tetraspan 3	1.71	Fibulin 1
2.13	Glycoprotein A33	1.70	Carcinoembryonic antigen-related cell adhesion molecule 3

T-cell activation

Increased in Chemotaxis		Increased in Fugetaxis	
5.76	Stat2 type a	4.71	MHC class II transactivator
3.22	Interleukin 21 receptor	2.65	T-cell receptor, alpha chain
2.20	T-cell, immune regulator 1	2.00	T-cell activation, increased late expression
		1.88	MKP-1 like protein tyrosine phosphatase
		1.72	T-cell receptor gamma constant 2
		1.70	T-cell receptor gamma locus

Migration related

Increased in Chemotaxis		Increased in Fugetaxis	
2.90	angio-associated, migratory cell protein	5.15	chemokine (C-X3-C) receptor 1
		3.24	EphA1 receptor
		2.40	ephrin-A5

FIGURE 10

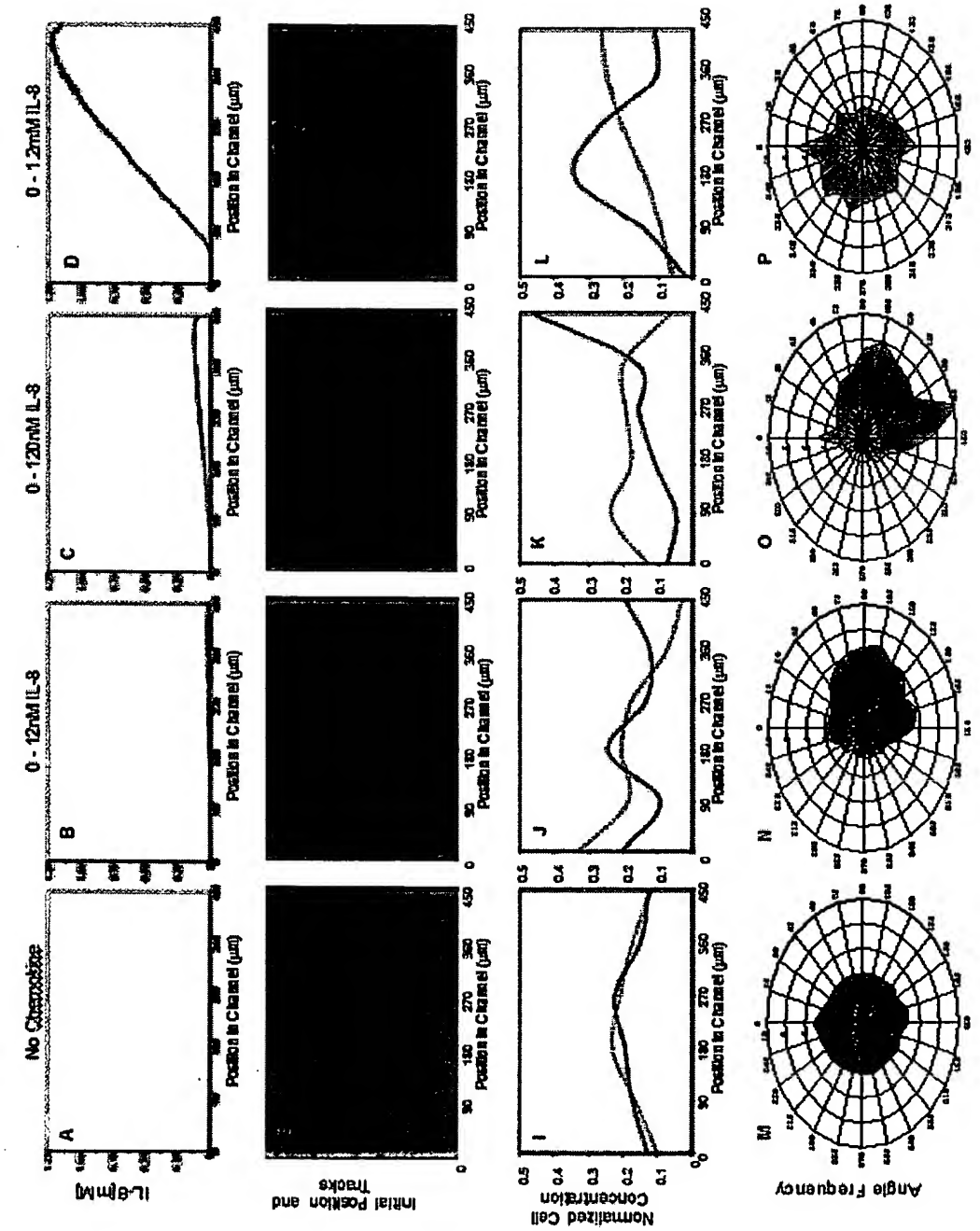


FIGURE 11

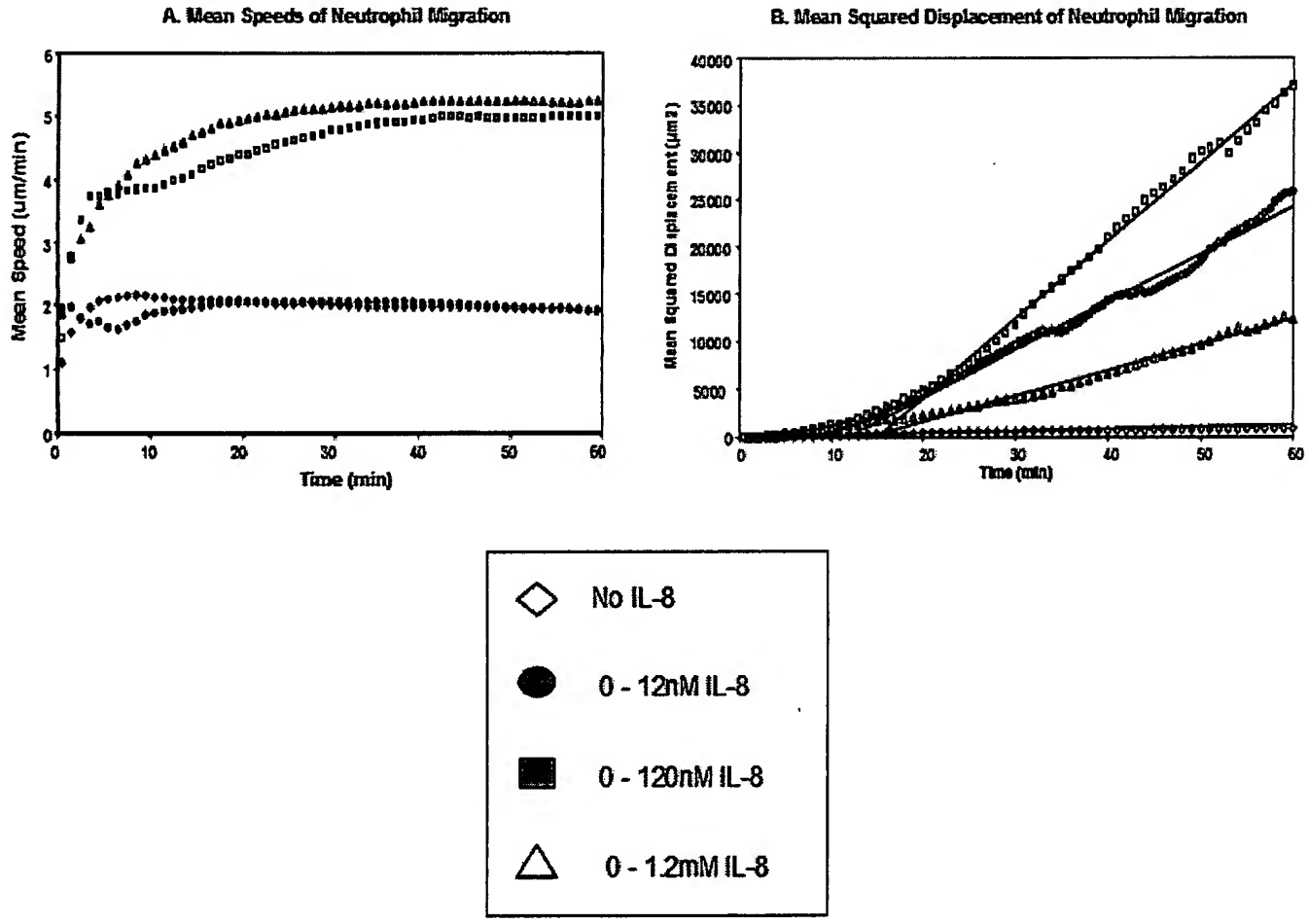
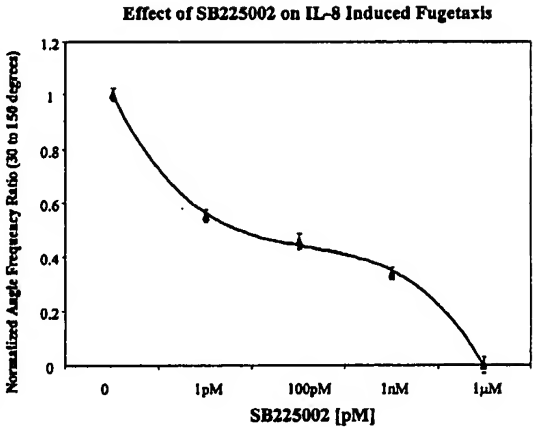
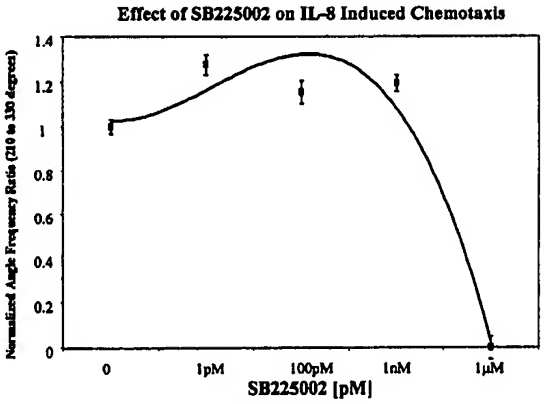

A. Mean Speeds of Neutrophil Migration
Mean Speed (um/min)
Time (min)
B. Mean Squared Displacement of Neutrophil Migration
Mean Squared Displacement (µm2)
Time (min)
No IL-8
0 - 12nM IL-8
0 - 120nM IL-8
0 - 1.2mM IL-8

FIGURE 12





[SB225002]	0	1 pM	100 pM	1 nM	1 μM
p-values FT vs CT	-	0.0037	0.0210	0.0036	0.4607

FIGURE 13

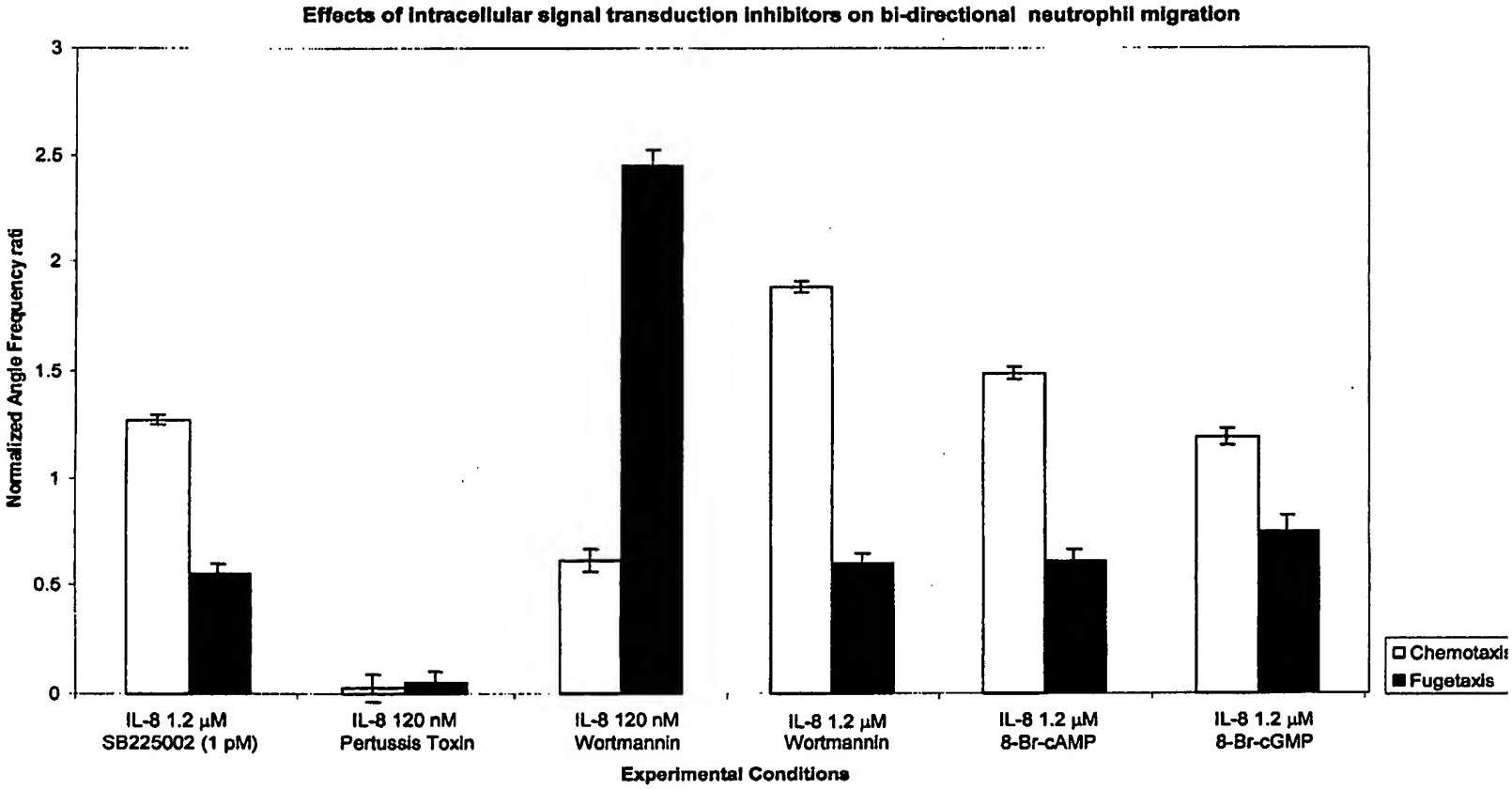


FIGURE 14

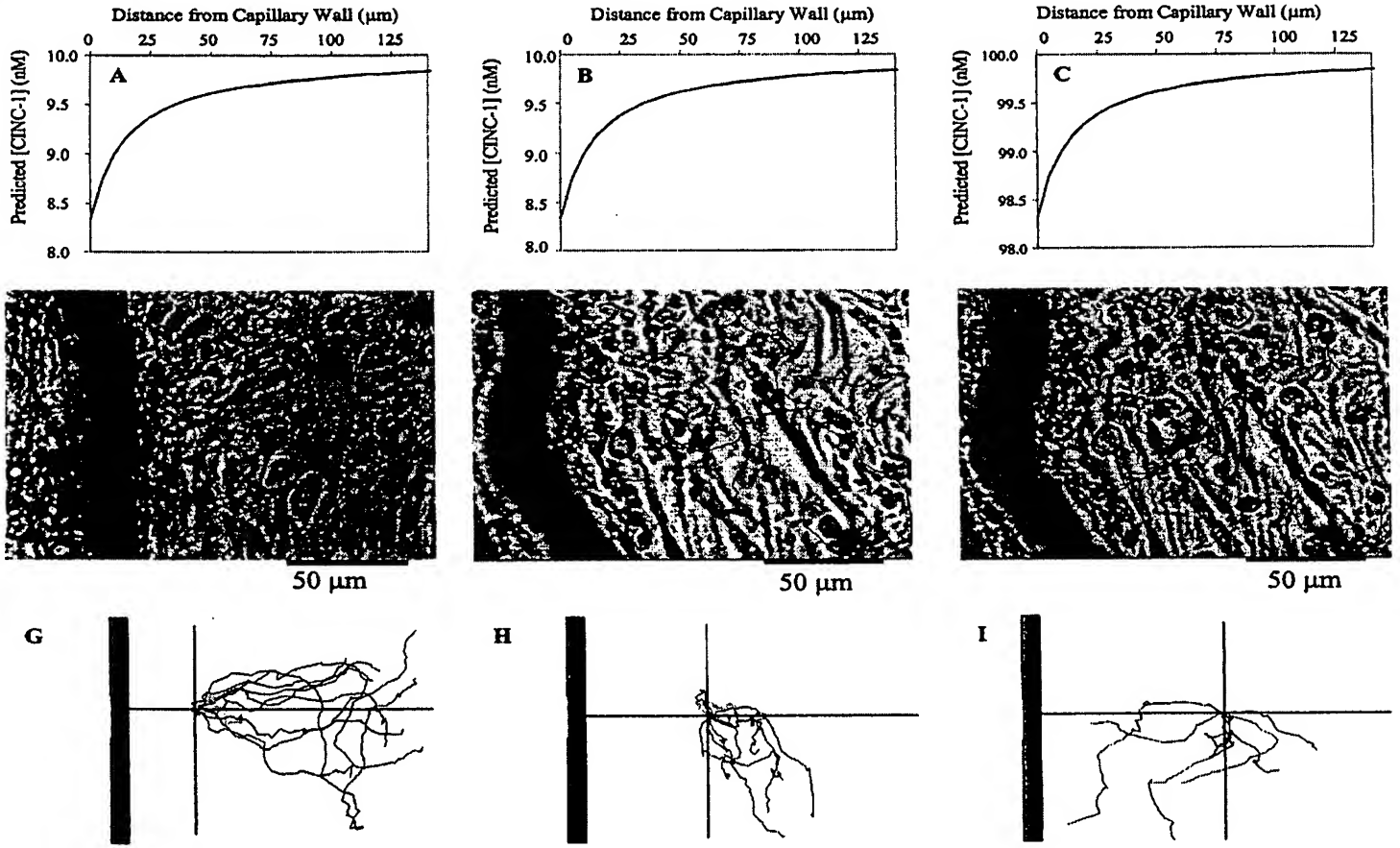


FIGURE 15
TABLE 8

Generated Gradient Parameters		Number of Cells	Mean Speed (μm/min) +/- SD	Random Motility Coefficient (μm^2/min)	Persistence Time (min)	Mean Chemotropism Index (MCI)	p-values (vs. no IL-8)	Sectional MCI (low, mid, high)	p-values Sectional MCI (low to mid, low to high, mid to high)
Peak [IL-8]	Gradient (Δ nM/μm)								
No IL-8	0	126	2.12 +/- 0.05	4.7	0	-0.02 +/- 0.01	-	-0.03, -0.03, -0.01	0.43, 0.15, 0.16
120 nM IL-8	0	50	4.13 +/- 0.89	34.7	4.5	-0.00 +/- 0.02	0.138	-0.00, -0.01, 0.02	0.48, 0.38, 0.37
12 nM IL-8	0.0267	75	1.96 +/- 0.05	168.7	21.5	0.32 +/- 0.03	< 0.0001	0.40, 0.28, 0.21	0.04, 0.01, 0.25
120 nM IL-8	0.267	87	4.77 +/- 0.06	217.9	21.8	0.39 +/- 0.03	< 0.0001	0.44, 0.42, 0.25	0.39, 0.001, 0.01
1.2 μM IL-8	2.67	80	5.10 +/- 0.04	67.2	10.9	-0.13 +/- 0.02	< 0.0001	0.20, -0.14, -0.22	< 0.0001, < 0.0001, 0.03

FIGURE 16
TABLE 9

Superfusion [CINC-1] (nM)	Number of Cell Tracks/steps Analysed	Mean Speed (μm/min) +/- s.e.	Random Motility Coefficient (μm^2/min)	Persistence Time (min)	Persistence Index +/- s.e.	Mean Chemotropism Index (MCI) +/- s.e.	MCI p-values vs (10 nM t0-90)
10	12/2160	7.71 +/- 0.63	127.45	4.27	0.55 +/- 0.08	0.51 +/- 0.08	-
10	6/1080	7.70 +/- 0.43	64.57	2.31	0.56 +/- 0.09	0.32 +/- 0.06	0.075
100	4/ 360	7.87 +/- 0.87	135.11	5.25	0.67 +/- 0.05	-0.35 +/- 0.12	< 0.0001

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